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SOME REMARKS ABOUT MATERNAL MORTALITY IN THE SOUTH

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MATERNAL mortality in the South is high. This high rate is in large part in negro women and in rural white women; those living below even a moderate subsistence level. Many factors make difficult an accurate study of maternal mortality in such women. I have long pondered the real situation. This study is in part an effort to clarify my own thoughts, and to try to obtain an accurate evaluation concerning the high maternal mortality in negro women.

My remarks have as a background the deaths of 97 colored pregnant women. All of these deaths occurred on our obstetric service at Grady Hospital in the city of Atlanta. The hospital is entirely charity and the only one available to a colored population of approximately 150,000. The service has accepted the hospital deaths of all pregnant women. The deaths were consecutive and no corrections were made. Deaths from ectopic pregnancy were not included.

The care of these women was beset with many difficulties, which those of you who have services in similar institutions can accurately evaluate. The complete service rendered these women was not the best. I feel sure, however, that it was much better than the average service received by negro women in the South. One statement can be made without equivocation; it was uniformly conservative. I might say here that the uncorrected mortality rate on our service is 5.6 per 1,000 pregnant women. This includes obstetric and nonobstetric deaths.

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In discussing preventability and assigning responsibility, I have followed no rule or formula. I have relied upon my obstetric judgment, my knowledge of the individual case, and whatever experience I might have gained from thirty years of such work. I did not find this analysis an easy task. I do not believe that any two men would get the same answer. From my analysis I have concluded that 52.5 per cent of these deaths were preventable. Lest we jump at conclusions, let me hasten to say that it is not a practical, workable percentage.

The responsibility for these preventable deaths was assigned as follows:

	PER CENT
Hospital doctor	37
Patient	37
Hospital routine	12
Outside doctor	10
Midwife	4

I confess to some astonishment at finding that patient and hospital professional staff share approximately an equal responsibility. However, I think that the largest truly preventable responsibility can be assigned to the hospital doctor. Perhaps I have been overcritical in determining our bad judgment, but if more leniency had been exercised, the figure would still have been too high. If we have such a large reducible factor in our own service where constant effort is made as to supervision and conservatism, it does not seem fantastic to speculate that probably 25 per cent of all colored maternal deaths can be prevented by the improvement of professional care alone. There is, of course, a certain irreducible figure, but so far as our service is concerned, a more constant and intensive supervision of the resident and intern staff would have told a different story.

Errors of commission on the part of the attending staff were relatively rare, errors of omission more frequent. During this period, the resident was given too much responsibility, oftentimes a responsibility requiring the judgment and dexterity of a larger experience. I am inclined to think that residents and interns on colored obstetric services are generally given more responsibility than they are capable of assuming and that this is a real cause for some of the obstetric deaths in colored women.

The preventability and responsibility as assigned to the patient is inaccurate, rather illogical, and requires discussion. A preventable percentage of 37 assigned to the great majority of negro women is an illusion. If we consider the ignorance and the poverty of the Negro race and all of the economic and social complications that go with ignorance and poverty, most of these deaths cannot now be prevented. Indifference is a larger factor than is realized. Many more years are needed to correct fundamental causes.

Granted that there is much room for professional improvement, considerable experience leads me to believe that a more sustained and permanent improvement must have as its background some education of all women.

The devastating mortality in the South is among the negroes and whites living below a subsistence level. This group does not fare so badly in larger cities with municipal hospitals, but even here, the rate would be considerably lowered by a better economic background. I am unable to see how good obstetric care can uniformly be given these women when such care is measured in terms of professional service alone.

I studied every record in this series, most of them several times. Approximately 30 per cent of these women did not die because of obstetric conditions. The causes of these nonobstetric deaths might be informative.

Uremia	8
Hypertensive heart disease	5
Pneumonia	4
Pulmonary tuberculosis	2
Miliary tuberculosis	1
Pulmonary embolism	1
Chronic nephritis	1
Rheumatic heart disease	1
Carbuncle of kidney	1
Esophageal stricture	1
Thrombosis cerebral artery	1
Peritonitis	1
Ruptured bladder	1
Spinal anesthesia	1

Uremia and hypertensive heart disease were the causes of approximately half the nonobstetric deaths. This was to be expected if one realizes the prevalence of chronic vascular disease in negro women. One wonders how many such deaths incorrectly diagnosed, creep into our southern rates. I realize that with some of these women it is difficult to determine whether pregnancy did or did not hasten death. Proper treatment of several of them would probably have delayed death, nevertheless, they are not obstetric deaths and they falsify our rates. Midwives do approximately 80 per cent of the colored obstetric practice in the South. Information concerning the nonobstetric deaths among these women is not accurate or sound and the statistics reported from such information are misleading and unfair. It is my opinion that 75 per cent of these nonobstetric deaths could not have been prevented regardless of any care that might have been given. Two were probably preventable, two refused advice, and as a result death was hastened, and pregnancy apparently hastened the death of three.

This study, as most similar ones, shows puerperal infection to be the "captain of death" for negro mothers. Nearly 60 per cent of the obstetric deaths were from sepsis. Abortal sepsis accounted for 40 per cent of all deaths from sepsis. Knowing that these were in a general municipal hospital, one immediately begins to question what was wrong and what the real cause behind such a staggering figure. Facts reveal what might be called obstetric helplessness. In 58.5 per cent of the women, the membranes had ruptured prior to admission. An equal percentage had fever when admitted. When first seen half of them had symptoms and signs of infection. Of the others, 25 per cent had definite pathology when first seen. Just one mother out of four who died of sepsis was ap-

parently normal when admitted. About one-third of the total number either delivered or aborted on the outside. The causes of death were:

Peritonitis	24
Bacteriemia	9
Bacteriemia and peritonitis	2
Sepsis	5

The fact that one-third of the septic women who delivered in the hospital were operated upon is questionable. There seemed to be a direct staff responsibility of about 12 per cent. Hindsight is better than foresight. Decisions were largely conservative, and if repetition were possible I do not see how they would be materially changed. The midwife and the outside doctor were relatively unimportant in this group. This is because the clinic during 1938 cared for 91 per cent of the colored obstetrics in the city and county. Only 64 live babies were delivered by midwives in 1938. Parenthetically, it is my opinion that, if colored midwives (bad as they are) were abolished under present conditions, colored maternal mortality in the South would immediately increase.

As chief of the service I am most concerned with the fact that I have attributed the primary responsibility for 15 per cent of the septic deaths to our hospital routine. This figure is not an accurate one, nor do I believe it is possible to get an accurate figure. But when apparently normal women enter the hospital and die of sepsis, the only honest conclusion one can reach is that infection probably occurred after admission. I feel sure that such women are a constant worry to every chief of obstetric service in a general municipal hospital. DeLee has said, "The environment has much to do with the causation of puerperal infection." There are general hospitals of good and bad obstetric environment. The lack of improvement of a poor environment is often not any fault of the professional staff. Constant effort, constant supervision, and uniform conservatism in a bad environment cannot prevent the occasional death from sepsis. I am reasonably certain that half of these deaths from sepsis were not preventable with the present economic and intellectual environment of the patients.

Though difficult to prove, I am certain that criminal abortions are rapidly increasing with the urban negress and were the cause of more than a fair percentage of the deaths in this group. There seems to be an idea, rather general, that the negro is a better obstetric risk than the white. She is on the average not a good risk, and is always a likely candidate for infection. There are any number of reasons why this is true. Perhaps the most important is her low resistance caused by an unbalanced and deficient diet. Marked anemia is frequent. The colored obstetric patient is most often stoical and likely to give one a false sense of security. Too often they do not have what it takes for a comeback after a long, hard labor. Superstitions, venereal infections, poor hygiene, and a pernicious environment are influencing factors.

Pre-eclampsia and eclampsia caused 23.5 per cent of the obstetric deaths. It is probable that the rate of death from the two diseases in colored women approximates 35 per cent. It seems worthy of emphasis

that 5 of these 16 women died of pre-eclampsia. Seven did not live twenty-four hours after admission, 2 delivered outside and 6 died undelivered. Five delivered spontaneously and 3 had forceps operations. Parenthetically, the diseases were not the indications for the forceps operations. There was one death from pernicious nausea and vomiting. Severe forms of this condition are rare in the negro. The responsibility for the deaths was charged to the staff in 4 instances, to the patient in 9, and to the midwife in 1. Speaking practically and so far as technical care was concerned, at least 50 per cent of these deaths were not preventable. Here again the uncontrollable factor is the patient, the old story of money and environment and the lack of realization of her responsibilities.

I believe that the major factor in southern obstetric mortality is the patient herself. In making this statement I am not trying to shirk professional responsibility. Obstetric mortality reports are likely to be misleading if not compiled from intelligent information. I am inclined to think that too much published data from our section of the country have been gathered without an accurate obstetric background. I do not see how there can be a sustained and substantial improvement in southern maternal mortality without a paralleled economic improvement.

Syphilis has a high incidence in the negro. It has been said that the disease has much to do with the high death rate of colored mothers. I do not believe that this is true. This study helps to substantiate my belief. One or more blood Wassermann tests were done on all but 8 of the women. Twenty per cent were positive, which is about the average figure found in pregnant negroes. Of the last 2,691 Wassermann tests done in our clinic, 21.5 per cent were positive. Only 5 of the 18 women with syphilis had chronic vascular disease, and in 2 of these the vascular disease was a contributory factor in the deaths. The environment that is largely the cause of such a high incidence of syphilis is the major cause of the high death rate in such women. The causes of death in these syphilitic women were:

Sepsis	8
Pre-eclampsia	2
Eclampsia	2
Ablatio placentae	1
Hyperemesis	1
Ruptured uterus	1
Pneumonia	2
Congenital heart failure	1

Hemorrhage was the cause, or was thought to be a contributory factor, in 12 of the 68 obstetric deaths. Two had delivered when admitted. An ablatio placentae, a cervical laceration, and a post-partum hemorrhage were directly the causes of 3 deaths. A more experienced house staff could probably have prevented these. A marginal placenta previa was probably a factor in one death and post-partum hemorrhage perhaps contributed to 9 others. Seven of the 9 died of sepsis and 2 of eclampsia. The loss of blood in our clinic is not measured but estimated. Perhaps hemorrhage was a larger contributory factor than I realized.

In the entire series, 25 per cent had some operation before, during, or after delivery. All but two of the operations were done in the hospital, most of them by an experienced obstetrician after due deliberation. If similar circumstances were repeated few of the procedures would be changed. The total operative incidence of our clinic in 5,000 consecutive deliveries, including abortions, is 3.96 per cent. This figure includes such simple procedures as packing the vagina. However, a critical analysis seemed to show that one-half were preventable, and in one-third the responsibility was placed with our professional staff. It was altogether too evident that more operative responsibility was delegated to the resident than he was capable of handling.

Four placentas were removed manually, two before admission and two after. All patients died of sepsis. Only one out of four of the women operated upon could have been called neglected when admitted. The operations done were:

Manual removal of placenta	1
Supravaginal hysterectomy	3
Breech extraction	2
Secondary abdominal pregnancy	1
Forceps delivery	5
Attempted breech extraction and extraperitoneal cesarean section	1
Hysterotomy and sterilization	2
Internal podalic version	1
Internal podalic version and manual removal of placenta	1
Dührssen's incisions and forceps	2
Craniotomy	1
Therapeutic abortion	1
Spinal anesthesia	1
Cystoscopy	1

Five died from the accidents of pregnancy and labor. One woman with an inverted uterus, who had been delivered by an outside doctor, was dead when admitted. Four died with ruptured uteri. One was cared for on the outside by a doctor, and another by a midwife; both died undelivered. One spontaneous rupture occurred during an apparently normal labor. The intern recognized the complication too late. The last was ruptured during a breech extraction which was done by a resident. This death should properly be assigned to the attending obstetrician.

So the story goes. A veritable hodge-podge of conditions and circumstances. Accurate evaluation seemed almost impossible. We doctors indisputably played an unenviable role. However, there are other problems that should be considered and must be solved before southern maternal mortality rates are comparable with those of other sections of the nation.

What inherent conditions, over which we physicians have no control, are in some measure responsible for our high maternal mortality rates? Webb, in his little book *Divided We Stand*, says, "The North and the South are about the same age. One had its cultural beginning in Massachusetts in 1620; the other made a start at Jamestown in Virginia thirteen years earlier. At that time there was not perhaps any great difference between the people of the two settlements. History and

tradition tell us that the one was Puritan and the other Cavalier; that one was stern and introspective and the other gay and zestful. Perhaps there were some differences in temperament and in inherited tradition, but these may be disregarded in the assumption that had the Puritan been set down in Virginia, he and his children would have become good Southerners, and had the Virginian been set down in Massachusetts, he and his children would as surely have become New Englanders."

The War between the States was devastating to North and South. The South paid a terrific economic price. But great as this was, it was not nearly so harmful as the political carpetbaggers that came later. The North held military and political control of the South until 1876. Today the North is the economic master of the South. This has not happened with the knowledge and abetting of the average northern citizen and no criticism is intended or implied. However the economic unbalance in the nation today is in large part due to this unbalance in the South. Economists say that it must be remedied before an average prosperity can be sustained.

Illiteracy is four times as prevalent in the South as in the rest of the Nation. The average expenditure on education per child is about half that of the country as a whole. To quote Webb again, "Illiteracy is explained by the presence of the negro in the South. But this is only an explanation. The fundamental reason is the lack of means. Beneath the ignorance of the South is not the will to be ignorant, nor an indifference to the advantages of education. It takes money to educate people, to pay teachers, to buy books from northern publishers, and to build the little red schoolhouse so dear to the vote hunting politicians. Let us recall that out of every 100 dollars deposits in banks, the South has less than 10. . . ." The South must educate one-third of the nation's children with one-sixth of the nation's school revenues. Teachers compare favorably with other sections; this in spite of the fact that the average annual salary of a teacher in Arkansas is $465 as compared to $2,361 in New York. The total endowments of all its colleges and universities are less than the combined endowments of Yale and Harvard. Our illiteracy is not the result of indifference. The South collects about half as much per person in taxes as does the nation as a whole, but she devotes a larger share of her income to schools. For the South to spend the national average per pupil, an additional quarter of a billion dollars per year would be required. Our economic masters do not pay their share of the cost of southern schools and institutions. The magazine *Look* in the issue of November 21, 1939, said, "For 70 years the South has been the victim of absentee ownership, adverse freight rates and tariffs. Today it is poor and ignorant, not because it wants to be, but because its economic masters have so decreed." Practically all of the money the South spends for insurance, automobiles, groceries, machinery, and other items too numerous to mention quickly leaves for parts unknown.

The average income in the South is half of what it is elsewhere. Comprising 28 per cent of the country's population, the South in 1934 paid about 12 per cent of the total income tax. This was $1.28 per capita and varied from 24 cents in Mississippi to $3.53 in Florida.

Nearly three-fourths of our population depends upon agriculture for a living. The average farm income in the South is $186 as compared to $528 elsewhere. Ever since the War between the States, the South has been the poorest section of the nation, despite the fact that nature endowed her with tremendous wealth. One-half of all farmers are tenant farmers, and their income is far below the southern average. Truly they are the peasantry of the United States. The South, with more than half of the farmers in the country, has less than one-fifth of the farm implements. More than half of all southern farmers depend upon cotton alone and cotton has long been an economic hazard. The one-crop system is changing, but the way is long and hard.

The South has less than one-third of the nation's farmland, but has 61 per cent of the land erosion. It loses each year more than $300,000,000 worth of top soil. Over 22 million acres of once rich land cannot be reclaimed. In the southeast an area as large as South Carolina has been gullied and washed away. It is estimated that in Alabama and Georgia alone 56,500 farm families are living on land too poor to support them under any system of agriculture.

The poorest rural area in America has the greatest number of people. The birth rate of the South exceeds that of any other region. It has a larger percentage of early American stock than any other region in the United States. The native born comprise 97.8 per cent of the population, of which 29 per cent are colored. There are 9 million negroes in the South, rapidly shifting to the larger centers, with probably one-half of them a liability to the community in which they live. Increasing competition for jobs has upset the balance of employment between white and negro, unemployed white people seeking and glad to get jobs heretofore held by negroes.

In the South there are fewer productive adult workers and more dependents per capita than elsewhere in the country. One child in eight, born and educated in Alabama or Mississippi, becomes an asset to some other state. Of all the eminent scientists born in the South, one-half are living elsewhere. Productive middle age groups leave the South in the greatest numbers, tending to make the South a land of the very old and the young.

Hookworm, malaria, and pellagra are real problems and public health work suffers from inadequate tax receipts received from a relatively small percentage of the people. In 1937 the average income from interest and dividends in the South was $17.55 as compared to $68.97 elsewhere. Too much of profit from southern industries goes to outside financiers in the form of dividends and interest. State taxation does not reach such moneys. Just as in education, the funds that are needed for public health smply are not available.

These pessimistic and gloomy conditions are not because we want them and not because we are not trying to improve them, however, I believe you will agree with me that such conditions are bound to influence maternal mortality.

Certain economic interests will in time correct many of them, but as Edwin R. Embree says, "There is danger here. What shall it profit the

South to multiply steel mills and cotton factories simply to become another South Chicago or Pittsburgh river front. What is the benefit of an increase in agriculture if it merely means that two stalks of cotton grow where one grew before, while the farmers starve. Why bigger schools if the children simply learn more rote lessons? Even better health is but little gain unless robust bodies house minds and souls. The South needs material betterment and there is every prospect that she will get it. But the great problem before the region is in getting possession of an abundance of things, to save her own soul. Let us stop pitying ourselves over the ravages of a war which was ended seventy-five years ago. Let us cease mourning over an ancient Golden Age which in reality was never very golden, which at best had but flecks of gilt scattered sparsely over great stretches of poverty, illiteracy and human exploitation. The glory of the South is not in the past but in the future."

I close with an optimistic prediction that is irrelevant to the subject discussed. This country's God-given heritage of liberty and democracy must be saved, and will be saved, largely by the conservative South.

NOTE: Much of the factual material was obtained from "A Report on Economic Conditions of the South" prepared for the President and from *Divided We Stand* by Webb.

THE THECA CONE AND ITS TROPISM TOWARD THE OVARIAN SURFACE, A TYPICAL FEATURE OF GROWING HUMAN AND MAMMALIAN FOLLICLES*

FOUNDATION PRIZE ESSAY

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THE ovary is the only gland with external secretion which does not have ducts or some permanent outlet. This is one of the anatomic differences between the ovaries and the testes. The latter possess a wide system of tubules and excretory ducts for the spermatocytes, while there is no similar provision made for the excretion of the ova from the ovary.

Ovulation, the delivery of the unfertilized ovum from the ovary, is a mechanical process governed by hormones as is childbirth, the delivery of the fertilized ovum from the uterus. In childbirth, on account of practical needs, the mechanical part of the process has been studied carefully. In regard to ovulation the opposite is the case. We know fairly well the endocrine stimulation, but the mechanical preparation has not been worked out sufficiently. In childbirth, we are dealing with a gross anatomic procedure, which can be readily studied and observed. In ovulation we are dealing with microscopic histologic changes which are difficult to interpret concerning their physiologic function.

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In the following report, we are not going into the endocrine side of the problem. Since the work of Zondek,[1] Aschheim,[2] Allen,[3] Hartman,[4] Novak,[5] and many others, the stimulating influence of the anterior lobe of the pituitary body has to be regarded as a well-established fact. Without this gland and its gonadotropic hormone there is no ovulation. This hormone (prolan A) stimulates the follicular growth.

In some animals (rabbits) who ovulate after cohabitation, a nervous stimulation of the hypophysis takes place which brings about an additional increase of the gonadotropic hormone. Within eight to twelve hours, this leads to the rupture of the follicle. In man and many other mammalians who ovulate independent of cohabitation, we have to admit "our ignorance of the exact hormonal factors concerned in ovulation" (Novak[5]).

However, as mentioned above, while lacking details, the fundamentals of the endocrine stimulation of ovulation can be regarded as well established.

Knowing the stimulating influence of the anterior pituitary, we take the rupture of the follicle for granted, not realizing that we are dealing with a mechanical process which requires definite anatomic histologic preparations. In regard to the Graafian follicle, one might feel that this is a cyst which must burst after it reaches a certain size and after the inside pressure becomes too great. If that would be a sufficient explanation, why do other cysts in the ovary, pathologic cystomas, etc., frequently reach the size of a child's head and more, and yet rarely rupture? There must be a histologic difference.

Before reporting our work and the resulting findings, we shall look over the explanation of the mechanism of ovulation in the literature.

In former days when endocrinology was an unknown field, many theories in regard to ovulation were developed.

Pflueger,[6] in 1859, believed that peristalsis of the ovary was a cause of ovulation. The action of smooth muscle fibers was supposed to bring about the rupture of the follicle. Henle,[7] however, in 1866, opposed this theory by showing that smooth muscle fibers accompanying major arteries in the ovary never extended into the ovarian stroma. Over sixty years later the muscular theory was revived by M. S. and R. F. Guttmacher,[8] in 1921, who described smooth muscle fibers in the theca externa of the follicle of swine. There is little histologic evidence for the action of smooth muscle fibers in ovulation. I have never found cells in the theca externa which could be considered as smooth muscle fibers.

Another theory of ovulation regarded active or passive hyperemia as the actual cause (Dahlmann,[9] Bayer,[10] and others). This idea goes back to the time when it was believed that menstruation and ovulation occurred at the same time, and has since been discarded.

A third theory concerned the possibility of enzymes being able to digest the internal lining of the follicle. Schochet[11] felt that there were proteolytic ferments in the liquor of the follicle. But, as pointed out by Smith,[12] there is very little direct evidence for their existence.

The most popular mechanical explanation of ovulation is that the increased pressure within the follicles precipitates expulsion of the ovum.

Koelliker,[13] in 1874, felt that a sudden increase of liquor production takes place which causes rupture of the follicle. Schaffer,[14] 1920, favored the same explanation.

Robert Meyer[15] has stated that the bursting of the follicle depended upon the relationship between the pressure inside of the follicle and the counterpressure of

the surrounding tissue. J. T. Smith,[12] as a result of very interesting experiments reported in 1937, found that there exists an increased osmotic tension in rabbit follicles after injection of pregnancy urine.

There is no doubt that the intrafollicular pressure plays a role in the final rupture of the follicle. To accept this fact, however, as the only explanation of the mechanism of ovulation is as much justified, as to accept the rupture of the membranes and the preceding osmotic tension within the uterus as a sufficient explanation for the mechanism of labor. The increased intrafollicular pressure can be accepted as a fact as proved by Smith.[12] This is, however, the very last phase which immediately precedes the bursting of the follicle.

Our problem is to establish the sequence of events which lead to this final stage. If we examine sections of ovaries of women and mammals, we find invariably the growing follicles deep in the ovarian stroma, while the primordial follicles are found close to the surface. How, then, do the follicles manage to return to the surface? As long as we cannot answer this question, we do not know why they finally rupture.

It has been my endeavor for a period of over eighteen years to study microscopically the histologic changes which culminate in ovulation.

I. THE RELATIONSHIP BETWEEN THE SIZE OF THE FOLLICLES AND THEIR DISTANCE FROM THE OVARIAN SURFACE

The first step in approaching our problem was to find out whether there exists a definite relationship between the size of the follicle and its distance from the ovarian surface.

Six normal ovaries from women between 20 and 41 years of age were cut in serial sections. Sixty-two growing follicles were observed. Their diameter was measured micrometrically as well as their distance from the ovarian surface where they were found nearest to the albuginea. Depending on the size of the follicles, 5 groups were formed (Table I), and the average distance from the ovarian surface calculated for each group. Primordial follicles were not included because they are in a resting stage and always found close to the surface. Follicles over 0.5 mm. diameter were not included, because in this group protrusion of the ovarian surface sets in, which makes measurement of their distance from the surface unreliable. All important changes take place in the groups from a diameter of 0.1 mm. to that of 0.5 mm. Table I shows the results.

TABLE I. SIZE OF FOLLICLE AND ITS AVERAGE DISTANCE FROM SURFACE OF OVARY

GROUP	SIZE OF FOLLICLE MM.	AVERAGE DISTANCE OF FOLLICLE FROM OVARIAN SURFACE MM.
1	Less than 0.1	0.65
2	0.1-0.2	0.82
3	0.2-0.3	1.3*
4	0.3-0.4	0.91
5	0.4-0.5	0.5

*Development of theca.

There is first a descent of the small follicles from the area of the primordial follicles into the ovarian stroma. The longest average distance (1.3 mm.) from the surface is reached in the third group. Here is the turning point. The next

group is found closer to the surface again. There is a typical ascent of the follicles in Group 4. Group 5 is found even closer to the surface than Group 4. Finally, follicles larger than those in Group 5 are visibly protruding over the surface.

How can we explain the descent of the small and the ascent of the large follicles?

The first movement, the descent of the small follicles, is a passive one which is easy to understand, since the ovarian cortex offers more resistance than the stroma. The growing little follicle, therefore, expands toward the hilus, following the line of least resistance.

The second movement, the ascent of the large follicles, is much more difficult to understand, because this movement is an active one which takes place against the resistance of the cortex. How is this brought about?

II. THE ECCENTRIC GROWTH OF THE THECA LAYERS

In Table I, we observed that the appearance of the theca layers coincided wth the ascent of the follicles. There are no theca layers in the two smaller groups. They are seen developing in the middle-sized group when the follicles have reached the deepest point in their migration. These theca layers when they first appear in growing follicles are equal at all sides. It is in this group that the formation of liquor sets in, usually in the peripheral pole of the membrana granulosa.

In the two larger groups, a decisive change takes place. There is a *one-sided thickness of the theca interna* present *at the upper hemisphere of the follicle.* In other words, the theca interna grows eccentrically toward the ovarian surface.

The closer the follicles are found to the ovarian surface the larger they are and the more outspoken is the difference between the wide theca interna at the upper hemisphere and the thin theca interna at the lower hemisphere, at the upper pole being finally eight to ten times wider than at the lower pole. This one-sided thickness of the theca interna is soft, because it consists of crowded, fast multiplying cells with many mitotic figures. The theca externa, on the other hand, is rich in tissue fibers and poor in cells and, therefore, hard. It is wide around the lower hemisphere of the follicle and thin at the upper hemisphere toward the ovarian surface, thus like a goblet keeping the growing follicle from expanding to any other side except where the soft and fast growing theca interna provides an area of lower resistance, which is toward the ovarian surface.

After these facts had been established in human ovaries, the third step was to study the ovaries of other mammalian orders, because we know that there is no important histologic feature in human beings which is not found in animals as well.

III. THE THECA INTERNA CONE

The one-sided thickness of the theca interna toward the ovarian surface was found in human ovaries. The first animal we used in order to study this condition in mammals was the cat. Twenty-two

cat ovaries were cut in serial sections for a total of 3,000 slides. New unexpected findings made it necessary to go over another set of 9 human ovaries, 3,000 serial sections being made.

After verifying the new findings in this group, the next step was to study ovaries from as many other mammalian species as we could obtain in the pre-estrus or estrus stage, which in larger animals was not always easy.

Together with an apprentice of mine,[19] I examined serially sectioned ovaries of horses, cows, swine, dogs, and rabbits. This represents a total material of 18,381 microscopic slides in four mammalian orders (Primates, Carnivora, Ungulata, Rodentia), which forms the basis of the following findings. Table II gives a survey of the material studied.

TABLE II. MAMMALIAN OVARIES EXAMINED

GENUS	ORDER	MICROSCOPIC SECTIONS NO.
Man	Primates	3,000
Cat	Carnivora	3,000
Dog	Carnivora	1,917
Rabbit	Rodentia	1,423
Swine	Ungulata	3,108
Cow	Ungulata	2,874
Horse	Ungulata	3,059
Total		18,381

The eccentric growth of the follicle and the one-sided proliferation of the theca interna toward the surface were verified in all mammalian orders examined.

The new phenomenon we observed seems to give us the final answer in regard to the ascent of the follicles to the ovarian surface.

The growing follicle develops a sprout much as a seed does. This sprout has a definite "tropism" toward the nearest point of the surface of the ovary. The one-sided proliferation of the theca interna proved to be only the base of the sprout. *The eccentric thickness was found by examining serial sections cut in different directions through the ovary. The conelike theca interna sprout is found in serial sections cut at a right angle to the surface.* In these slides one finds that the proliferation of the theca interna forms a cone which has a triangular wedge-shaped cut surface, its axis always pointing to the ovarian surface.

I shall now proceed to illustrate the *theca interna cone,* as I have named this structure, in small, medium, and large follicles of various mammals including man. We found the theca cone in all mammalian ovaries which we examined. Since we studied four mammalian orders which all showed the theca cone, we feel entitled to present this feature as typical in the normal histology of the ovary.

In pictures not showing the ovarian surface, the area of primordial follicles will always represent the cortex, in other words, the direction toward the surface.

The *smallest follicle with a theca cone* was found in a rabbit (Fig. 1). A group of about twelve theca cells forms a triangular roof on top of the limiting membrane which includes just one row of granulosa cells and the ovum. This follicle has otherwise no theca at all. While the ovarian stroma surrounds this young growing follicle at all other sides as it does the adjacent primordial follicles, a group of cells with bigger nuclei and different in shape and arrangement at the upper hemisphere form a triangular wedge. The axis of this cone points toward the area of the primordial follicles. This is the beginning of the theca cone.

The *next group of follicles* shows the theca cone more distinctly. Fig. 2 illustrates a small follicle of a cat. The granulosa has grown into several layers of cells. The follicle becomes elliptic in this phase because the granulosa grows faster at the upper and the lower poles than at its sides. In the peripheral pole, the formation of the liquor is just beginning. On top of this peripheral pole, the theca

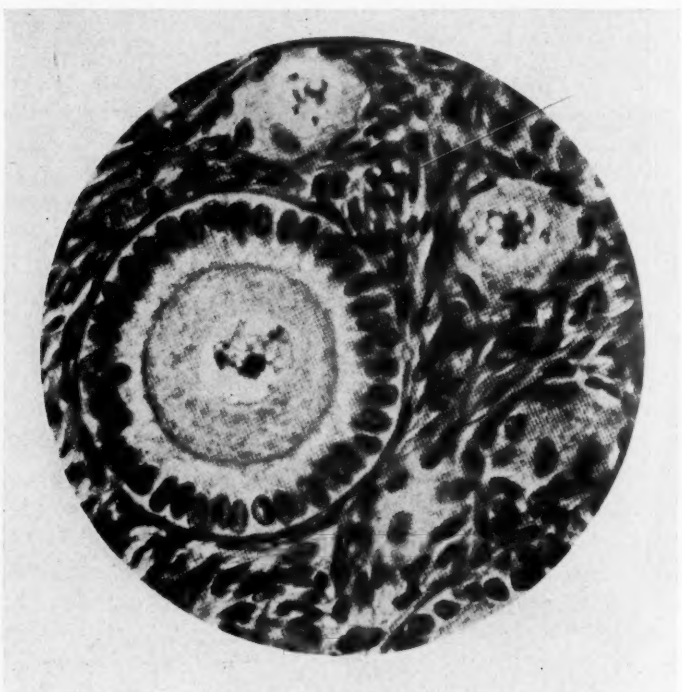

Fig. 1.—Theca interna cone, first stage. Triangular thecal wedge, indicated by line, pointing toward ovarian surface. No theca layers around follicle otherwise, one layer of granulosa cells. Small follicle of a rabbit (×325).

interna cone is present. There are no theca layers to be found at any other part of the follicle. The theca cone consists of cells in size and shape different from ordinary stroma cells. They show more cytoplasma and big round nuclei. They form a triangular wedge its axis pointing toward the region of the primordial follicles which is the cortex.

Fig. 3 illustrates a small follicle of a rabbit with the same shaped theca interna cone on top of the peripheral pole. It is noticeable that the theca interna is now present all around the follicle. The follicle is larger than that in Fig. 2. The granulosa has multiplied into many more layers. The theca cone is dark because of its crowded cells and nuclei. It pushes the surrounding tissues aside and grows infiltrating toward the area of the primordial follicles, i.e., the ovarian surface.

In the group of *medium-sized follicles,* one observes the effect caused by the one-sided proliferation of the theca interna. These cells infiltrate like the chorio-epithelium of the placenta. They penetrate the ovarian stroma pushing it aside,

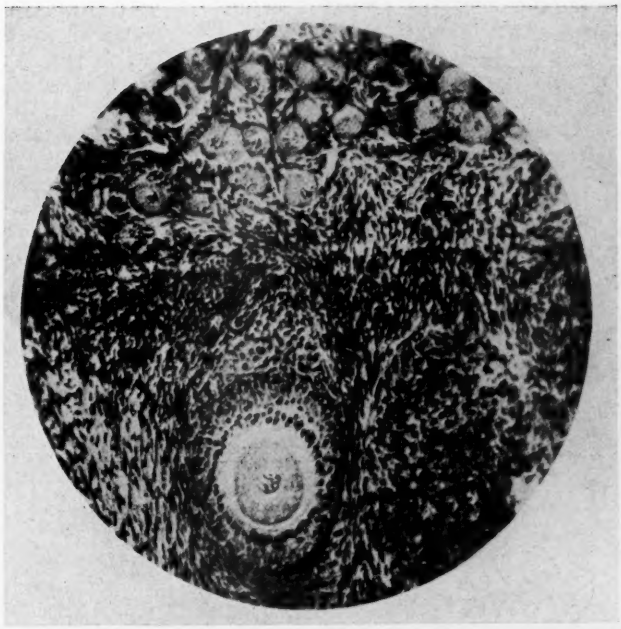

Fig. 2.—Theca interna cone, second stage, pointing toward ovarian surface. No thecal layers around follicle otherwise. Two-three layers of granulosa cells. Small follicle of a cat (×160).

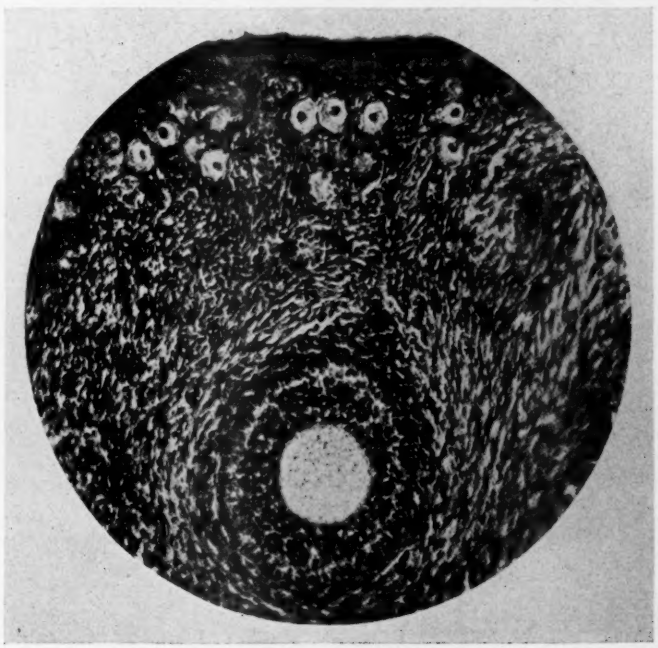

Fig. 3.—Theca interna cone, second stage, pointing toward ovarian surface. Beginning development of theca layers around follicle. Multiple layers of granulosa cells. Small follicle of a rabbit (×100).

causing a streamlike adaptation of the surrounding connective tissue by ploughing a path for the expanding follicle. The theca cone provides, at the same time in its rear, an area of lower resistance for the follicle which follows the axis of the theca cone by expanding into the cone as soon as the liquor formation permits the follicle to become cone-shaped itself.

Fast growing tissue rich in cells is soft. The theca interna cone is such a formation. The follicle is surrounded otherwise by dense connective tissue, rich in fibers, and, therefore, hard (theca externa). The growth of the granulosa and the production of liquor requires an outlet. This is provided by the theca interna cone in the direction toward the ovarian surface. We now can explain why in this phase of follicular development the distance between follicle and ovarian surface decreases. The growth of the theca interna toward the ovarian surface is an active infiltrating one. The growth of the granulosa toward the surface is not infiltrating, because it is always surrounded by a limiting membrane, which permits adaptation

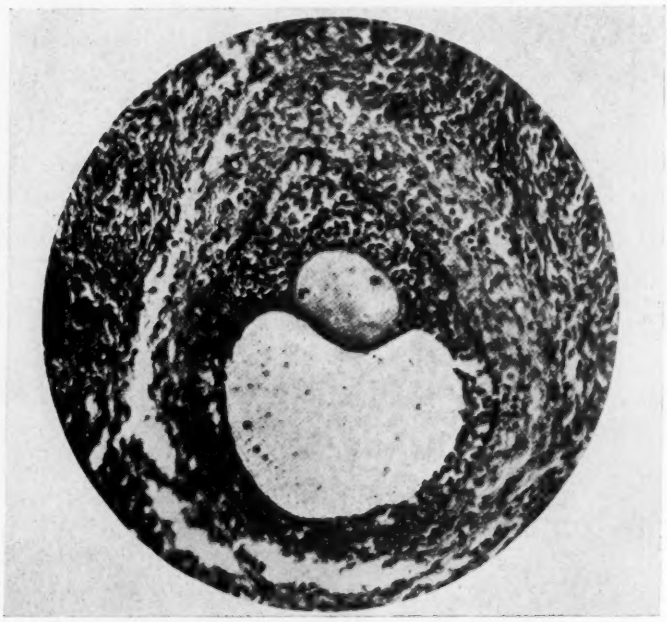

Fig. 4.—Theca interna cone, third stage. Granulosa protruding into theca cone. Appearance of liquor. Human follicle (×160).

into the cone, but keeps granulosa, liquor, and ovum separated from the theca layers. The adaptation of the follicle proper into the cone is found best when the ovum is located in the upper hemisphere of the follicle. The granulosa grows faster around the ovum than at other parts. It shows more mitotic figures at the cumulus ovigerus. It is, therefore, softer and more adaptable here.

An example is Fig. 4, showing a human follicle with the ovum located in the upper hemisphere. The theca cone is fully developed. *Protruding into the theca cone is the granulosa which becomes cone-shaped itself. The axis of the theca cone and that of the granulosa cone coincide.*

Fig. 5 illustrates the same conditions in a follicle of the cow. The theca interna in both pictures is cone shaped as is the granulosa, which follows the axis of the theca in the direction toward the ovarian surface.

In rabbits and in swine, we found a peculiarity which seems to be an additional help in the ascent of the follicle. The surrounding connective tissue undergoes a marked edematous softening which is more outspoken around the theca cone than at other parts of the follicle.

This edema made us wonder as to whether the cells of the theca interna cause destruction or necrosis of the surrounding tissues; in other words, whether the thecal wedge ploughs its way not only mechanically but also chemically, by digesting or dissolving cells of the stroma. By applying the Mallory and Azan stain we tried to determine the presence of such enzymes. The results were negative. I did

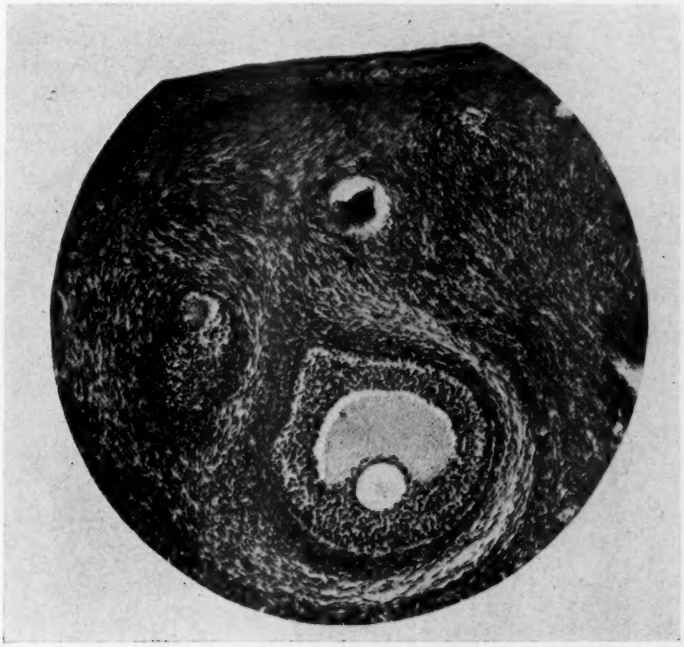

Fig. 5.—Theca interna cone, third stage, and granulosa cone, coinciding axis pointing toward ovarian surface. Streamlined adaptation of stroma. Ascending follicle of a cow (×80).

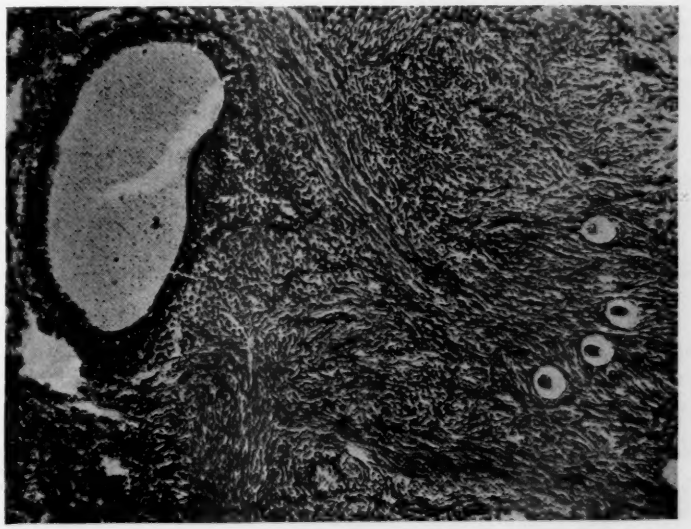

Fig. 6.—Theca interna cone and granulosa protruding in same axis toward ovarian surface. Streamlined adaptation of stroma. Ascending human follicle (×80).

not observe any chemical action, lysis of cells, or destruction of nuclei. The ascent of the follicle seems to be brought about by mechanical changes only, which, of course, are stimulated by endocrines.

Fig. 6 illustrates a human follicle with a fully developed granulosa niche protruding into the theca interna cone. It is noteworthy that both formations have the same axis pointing toward the cortex of the ovary which, in this picture, as always, is recognizable by the area of primordial follicles.

As a typical example of the *group of large follicles,* one can take that of a cat illustrated in Fig. 7. On account of size, only the upper part is photographed. Two atretic follicles lie in the way of the maturing one. One notes with what strength the theca interna wedge is preparing the path for the ripening follicle between the two atretic structures by pushing them aside.

It is not necessary to show the same illustrations for the various mammalian species. The larger the animal, the larger is the ovary, and the more marked is the thecal wedge and the granulosa protrusion into the thecal cone. In small animals, such as mice, the ovaries also are small, and the follicles are near the surface. There is no need for much action of the theca interna, because development takes place right below

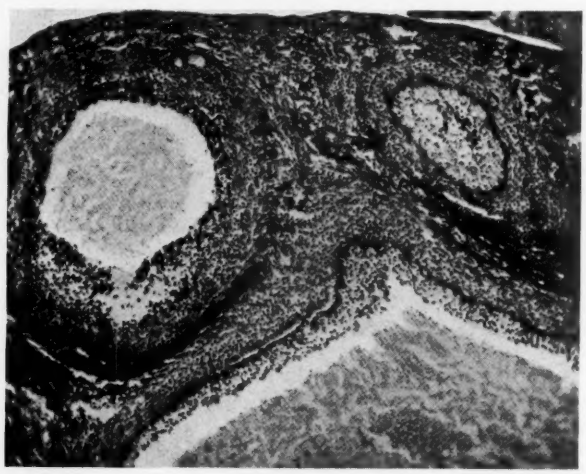

Fig. 7.—Theca interna cone and granulosa protruding toward surface of ovary, pushing aside two degenerated follicles. Large ascending follicle of a cat (×60).

the surface of the ovary. Therefore, I did not see very marked formation of a wedge in the ovaries of mice. In the slightly larger animals, the rabbit for example, the formation of the theca cone was very well developed. Likewise, all the others, without exception, exhibited well-developed formation of the theca cone.

IV. THE ROLE OF THE THECA CONE IN OVULATION

Particularly interesting were the findings in horses, because they gave us the opportunity of determining whether our opinion concerning the significance of the theca interna cone was correct. While in other mammals the ovaries have an entirely free surface which permits ovulation to occur at any place, the ovary of the horse is surrounded by mesovarium, leaving only one little spot free, the ovulatory fossa, where ovulation takes place.

In all other mammals studied the theca interna cones grow divergently toward the nearest point of the ovarian surface. In horses we found the theca interna proliferating convergently toward the ovulatory pit, thereby giving evidence that the theca cone has the special function of bringing the follicle up to that part of the ovarian surface where the ovum can enter the peritoneal cavity.

Fig. 8 illustrates a medium-sized follicle of a horse. The theca interna cone is fully developed. The granulosa is protruding into the cone in a very distinct manner, indicating the direction the follicular expansion is going to take. The axis of this cone plus granulosa protrusion is pointing toward the ovulatory pit. This was verified by going over the entire series of sections.

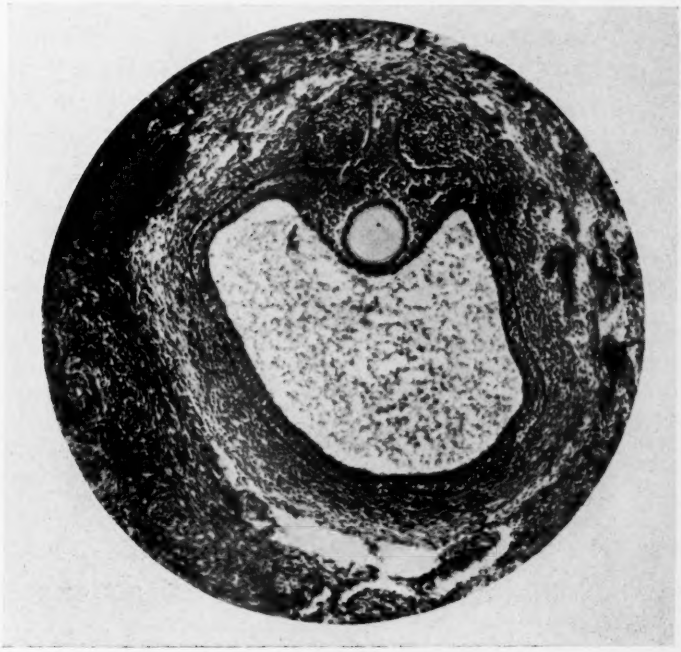

Fig. 8.—Ascending follicle of a horse. Theca interna cone and granulosa protrusion following the cone axis (×60).

Fortunately, we were able to prove the convergent growth of horse follicles and their theca cones, by showing a photograph of two growing follicles in one microscopic section. Horses ovulate rarely and the incidence of twins is less than in man. It is, therefore, hard to get horse ovaries in the pre-estrus stage, and it is even harder to find two growing follicles close together in one microscopic slide. We felt, however, that we should not stop before finding this combination, because it should be regarded as the final proof that the theca cone has the task of bringing the follicle up to that part of the ovarian surface where ovulation can take place.

The convergent growth of the thecal cones toward the ovulatory pit in horses and the divergent growth of the thecal cones in all other

mammals toward the ovarian surface indicate that this is the mechanism by which the ascensus of the follicles is brought about.

When the ascent of the follicle through the ovarian stroma and the cortex is completed, protrusion commences. The theca interna cone flattens out, forming first a straight line and finally disappearing entirely. Proliferation of the theca plus granulosa ceases, and the membrane between the interior of the follicle and the peritoneal cavity becomes progressively thinner. Circulation on top of the vertex of the Graafian follicle is interfered with by internal pressure. The capillaries do not contain blood cells any more. Atrophy sets in at the stigma. The opening of the follicle takes place in a very smooth manner, almost always without any bleeding.

After ovulation has occurred, the follicle collapses and the walls begin to form the corpus luteum. One cannot confuse the theca interna cone of intact growing follicles with the changes of the theca interna in follicular degeneration if one observes the following differences:

1. *The theca interna cone is present only at* one point of the follicle which is always *the vertex of the peripheral hemisphere* and closest to the free surface of the ovary. The transformation of the theca in degenerating follicles is observed at all sides.

2. Within many cells of the theca interna cone are *numerous mitotic figures,* seen on high power of magnification (hyperplasia). Among the cells of the theca interna in degenerating follicles almost no mitotic figures are seen; instead the change is one of hypertrophy, owing mostly to infiltration of fat.

3. The cells of the *theca interna cone* form a *solid closed formation.* Only the uppermost cell groups are occasionally surrounded by connective tissue fibers. The cells of the luteinized theca are arranged in groups throughout by septa of connective tissue.

4. Finally, if there is any doubt, *examination of the ovum and the membrana granulosa* always will make evident whether we are dealing with an intact follicle or a degenerated one.

V. GEOMETRIC CONSIDERATION AND PHOTOGRAPHS OF THE THECA CONE IN THE LITERATURE

After the theca interna cone and its significance for the ascent of the follicles have been demonstrated in human and mammalian ovaries, the question arises as to why a typical histologic process such as found in all the mammalian orders examined has not been discovered previously in an organ thoroughly investigated for many generations.

A simple mathematical consideration may explain the situation (Fig. 9).

The cut surface of a sectioned cone appears triangular in shape only if the section passes through the apex of the cone and if its axis coincides with that of the cone, represented by line *I.*

If sections through a follicle are parallel to the ovarian surface, represented by line *II,* we obtain Fig. 9, *b.* All layers of the follicle appear equal on all sides. The thecal wedge would not show in any serial sections containing the cavity of the follicle.

If sections are made obliquely through the follicle, represented by line *III,* we obtain Fig. 9, *c;* this would show only the one-sided thickness of the theca interna and not the wedge. This would hold true only for part of the sections.

If the sections are made perpendicular to the surface of the ovary, we obtain various outlines of the follicle. A section through line *IV* would look like Fig. 9, *d*. We may visualize the eccentric growth of the theca interna, not the wedge.

Only if the section is perpendicular to the surface of the ovary and passes through the apex of the cone represented by line *I is there a chance to obtain a cut surface showing the triangular shape of the wedge of the theca interna* (Fig. 9, *a*).

This is the reason why we discovered the eccentric growth of the theca interna first. It could be observed more easily than the wedge. The latter could be demonstrated only under favorable conditions. The chance of missing it, even in studying serial sections, is hundreds of times greater than the chance of finding it. This very fact made it necessary to examine a considerable number of ovaries cut in serial sections from various mammalian orders before we were convinced that we were dealing with a typical physiologic process in the normal histology of the ovary in human beings and mammals.

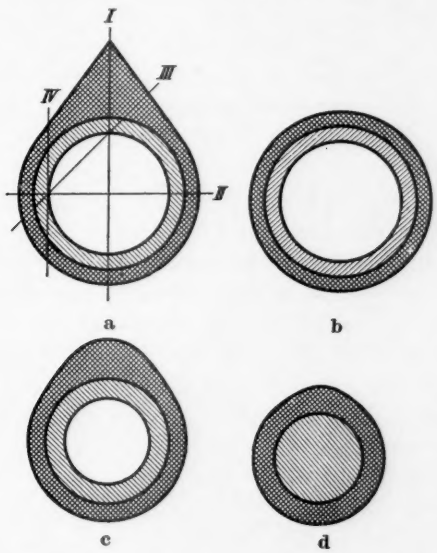

Fig. 9.—Schematic outline of follicle with theca interna cone. Figures *a*, *b*, *c*, and *d* are obtained when follicle is cut following lines *I*, *II*, *III*, *IV*, respectively.

In going over the literature, we found that the theca cone has been photographed and published by other authors who did not realize they had something of importance in their pictures.

First, I have to confess that I am guilty myself. In one of my early papers I pictured a small growing human follicle with a pointed triangular theca interna cone, not realizing that I had the answer to my problem right there (Fig. 3 in reference 17, p. 184).

Recently, I found in B. Zondek's book[1] (page 21), in Fig. 5 which illustrates a human ovary, a small growing follicle with a perfect theca interna cone, pointing toward the area of the primordial follicles.

In J. T. Smith's paper,[12b] I found another photograph showing theca cones in two rabbit follicles. His Fig. 2, in a very distinct way, illustrates not only the theca cones in both growing follicles but also the edema which we described above

as a peculiarity in rabbit follicles. The tropism of the theca cones toward the ovarian surface in this picture is evident, since the ovarian surface is visible.

I mention the photographs found in the literature in order to explain that the theca cone is not hard to find after knowing of its existence and significance.

VI. THE THECA CONE AS A TEST FOR GONADOTROPIC HORMONES

After presenting the theca cone and its role in ovulation as a typical feature in the normal histology and physiology of human and mammalian ovaries, the question arises as to whether this knowledge may be of any practical value in our clinical work.

The presence of gonadotropic hormones is indicated by their follicle-stimulating influence. Preparations of gonadotropic hormones are tested by their faculty to stimulate follicular rupture and corpus luteum formation in infantile female animals. In these tests (Aschheim-Zondek test in mice and Friedman test in rabbits) hemorrhage occurs within the follicles. This bleeding is unphysiologic. As mentioned above, normal ovulation occurs without hemorrhage. We know that we are dealing with unphysiologic amounts of gonadotropic hormones if we obtain hemorrhage.

In regard to the diagnosis of pregnancy, we are not interested as to the quantity of hormones the test animals may require for normal ovulation. In regard to the treatment of human beings, however, the quantity of gonadotropic hormones plays an important role. The work of Davis and Koff[16] indicates that the preparations made from pregnant mare's serum are able to stimulate ovulation in man.

Ovulation with hemorrhage means overdosage. We need a test indicating various degrees of follicular stimulation, not only the final stage of follicular rupture. Here may be a place for the theca interna cone as a test for gonadotropic hormones.

The theca cone is found in actual growing follicles only. It is never present in primordial follicles. It is not found in resting follicles if there is such a stage at all. It disappears as soon as degeneration sets in. In other words, it is a sign of actual development of a follicle. It, therefore, may be useful as a test for the presence and quantity of gonadotropic hormones.

We have started animal experiments to determine the time necessary for the theca cone to develop and the time required to bring the follicle to the ovarian surface under normal and artificial stimulation. The results may give us a more detailed picture in regard to the dosage of gonadotropic hormones necessary to obtain physiologic follicular growth and ovulation.

SUMMARY

This paper is a report of microscopic work done over a period of over eighteen years (1921 to 1940). It presents the "*theca interna cone*" and its tropism toward the ovarian surface as a new feature in the normal histology and physiology of the ovary. The theca interna cone

functions as a pathmaker for the ascent of the growing follicle to the ovarian surface. It, therefore, is an integral part of the mechanism of ovulation.

The findings are based upon over 18,000 microscopic serial sections of ovaries in four mammalian orders: Primates (man), Carnivora (dog, cat), Rodentia (rabbit), Ungulata (horse, cow, swine), and illustrated by photomicrographs showing small, medium, and large follicles of various species.

1. The diameter of human growing follicles and their distance from the ovarian surface were measured micrometrically. Corresponding to the size, five groups of follicles were formed, and the average distance of each group from the ovarian surface was calculated. It is shown that in the early stages of follicular growth, up to a diameter of 0.25 mm., there is a descent of the follicles from the albuginea toward the hilus, and that there is an ascent of the larger follicles back to the surface. This ascensus begins with the appearance of the theca layers.

2. Examination of the theca layers in serial sections shows that their growth is an eccentric one. There is present a one-sided thickness of the theca interna, rich in cells, toward the ovarian surface, which in large follicules is from eight to ten times wider at the upper pole than at the lower pole toward the hilus. The theca externa, on the other hand, rich in connective tissue fibers, is wide around the lower hemisphere of the follicle and thin at the upper hemisphere toward the ovarian surface. Thus, the theca externa, like a goblet, keeps the follicle from expanding to any other side except to the surface of the ovary.

3. In serial sections cut perpendicularly to the ovarian surface, it is found that there is not only a one-sided blunt thickness of the theca interna but a wedge-like "theca interna cone" with a triangular cut surface which always points to the nearest part of the ovarian surface. This theca cone possesses a tropism toward the surface like the sprout of a seed and plows the path for the follicle by active infiltrating growth through the stroma and albuginea. The follicle proper follows the line of least resistance provided by the theca cone. The granulosa protrudes into the cone, frequently adopting the shape of a cone itself, the axis of which always coincides with the axis of the theca cone.

4. The theca cone is found in all mammalian species examined, including man. In all mammalian species with a free ovarian surface, the theca cones grow divergently toward the next point of the ovarian surface. In horses where the ovaries are surrounded by connective tissue, the theca cones grow convergently toward the only free spot, the "ovulatory pit." This proves that the theca cone fulfills the purpose of bringing the follicle to that part of the ovarian surface where ovulation can take place.

5. Geometric considerations show that the theca interna cone can be demonstrated as a triangular-shaped wedge only in serial sections which are cut perpendicularly to the ovarian surface and which run through the apex of the cone. Sections cut in any other direction will never reveal the theca cone as a wedgelike formation. This must have been

the reason it has not been found before in the ovary, an organ which has been studied by many research workers for several generations.

6. The theca interna cone is present in actually growing follicles only. It disappears as soon as degeneration takes place. It, therefore, can be used as a test for gonadotropic hormones. Rupture of the follicle is useful as a qualitative test, but, if combined with hemorrhage, shows overdosage of gonadotropic hormones. The theca interna cone can be useful as a quantitative test, showing the various degrees of stimulation before ovulation occurs. It, therefore, should become useful for determining the physiologic dosage and timing.

Figs. 1, 3, 5, and 8 are photographs from specimen observed with Erika von Moellendorff, at Paul Strassmann's Clinic, Berlin.

Figs. 2, 4, 6, and 7 are photographs from specimen observed at Paul Strassmann's Clinic, Berlin.

This work was done: (1) in the Pathologic Institute of the University of Freiburg, Germany (1921 to 1922);[17] (2) in the Frauenklinik of Prof. Dr. Paul Strassmann, Berlin, Germany (1922 to 1932);[18] (3) at the University of Berlin, Germany (1932 to 1936);[18, 19] (4) at the Mayo Clinic, Rochester, Minnesota (1936-1938);[20, 21] (5) at Houston, Texas (1938 to 1940).[22]

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DEEP CAUTERIZATION OF THE CERVIX*

A Factor in Reducing the Mortality of Hysterectomy. A Six-Year Survey

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HYSTERECTOMY is one of the more common gynecologic operations, and a most useful one, so that every effort should be made to reduce the mortality and morbidity to as low a rate as possible.

There has been much discussion as to the relative merits of subtotal and total hysterectomy, and which operation is preferable in benign conditions. Formerly total hysterectomy had been reserved almost entirely for malignant disease, but in the last fifteen years or more, total hysterectomy has been strongly advocated in some clinics for benign conditions of the uterus, largely because of the hazard, present and future, offered by the infected cervix.

Table I. Mortality Associated With Supravaginal Hysterectomy in Various Clinics

	NO. OF CASES	MORTALITY PER CENT
Schmitz	3,129	2.1
Pearse	1,900	1.7
Read and Bell	1,739	2.1
Newell	1,307	3.8
Siddall and Mock	1,141	2.6
Greenhill	1,408	4.6
Amreich	1,253	1.6
Fullerton and Faulkner	609	4.4
Faulkner	653	2.3
Counseller	487	1.9
Mathieu	472	1.9
Danforth	304	0.28
Samuels and Edlavitch	303	2.6
Fletcher Shaw	232	3.05
Masson	217	1.8
Burch and Burch	166	4.2
Dupertuis and Zollinger	755	1.6
Total	16,165	2.5 Average

MORTALITY

Among 16,147 cases reported by 17 authors (Table I) the average mortality was 2.5 per cent for subtotal hysterectomy. Newell and Scrivener,[1] in a review of the literature for a five-year period, found that in 14,280 subtotal hysterectomies reported, there was a minimum mortality of 1.2 per cent and a maximum mortality of 4.7 per cent. In 5,223 total hysterectomies there was a minimum of 1 per cent and a maximum of 7.9 per cent mortality. Masson[2] states that,

*Read at the Fifty-Third Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., September 26 to 28, 1940.

"statistics show that in an unselected group of cases in which operation is advisable and is performed by a member of the visiting staff of most accredited hospitals, the mortality rate associated with subtotal hysterectomy is about 4 per cent, and 6 per cent for total hysterectomy." He reports, however, a mortality of 0.9 per cent in 766 subtotal hysterectomies at the Mayo Clinic in a five-year series and a personal mortality of 0.76 per cent in 784 hysterectomies, 196 of which were vaginal hysterectomies with a mortality of 0.51 per cent. Smith[3] also reports a mortality below 1 per cent for subtotal hysterectomy at the Evanston Hospital, 0.5 per cent for all hysterectomies, and 0.8 per cent for the subtotal operation.

A six-year survey, which forms the basis of our study, is shown in Table II. It includes all the ward and private patients of the Gynecological services of the Elizabeth Steel Magee Hospital and St. Francis Hospital in Pittsburgh, for the six-year period from May 1, 1934, to May 1, 1940. These operations were performed by 36 surgeons, including the residents. There were 1,640 hysterectomies and 1,464 of these were subtotal hysterectomies, with 28 deaths or a mortality of 1.91 per cent. Included also are 116 total hysterectomies with 5 deaths or a mortality of 4.31 per cent. Sixty vaginal hysterectomies were done with 2 deaths or a 3.33 per cent mortality. The gross total mortality for all cases is, therefore, 2.31 per cent.

TABLE II. TYPE OF HYSTERECTOMY AND MORTALITY

TYPE	NUMBER		DEATHS		PER CENT	
	AUTHORS' CASES	TOTAL SERIES	AUTHORS' CASES	TOTAL SERIES	AUTHORS' CASES	TOTAL SERIES
Supravaginal	442	1,464	2	28	0.45	1.91
Total	53	116	4	5	7.5	4.31
Vaginal	19	60	0	2	0.0	3.3
Gross totals	514	1,640	6	35	1.16	2.13

Out of the total series of hysterectomies, 514 were done by the authors in consecutive, unselected, private and ward cases (Table II); 442 of these were subtotal hysterectomies with 2 deaths or a mortality of 0.45 per cent. We also did 53 of the 116 total hysterectomies with 4 deaths or a mortality of 7.5 per cent. Nineteen vaginal hysterectomies of the 60 performed were our own, and we had no deaths. Therefore, out of 514 cases our gross mortality is 1.16 per cent.

Of the entire series, there were 1,344 cauterizations preceding hysterectomies, or 82 per cent of all cases, though most of them were in the subtotal group, and of these there is a mortality of 1.1 per cent. In the subtotal group, there were 196 cases without cauterization. Thirteen of these patients died, a mortality of 6.5 per cent. The mortality of the cauterized cases was 1.18 per cent. Therefore the mortality percentage in subtotal hysterectomy was five and one-half times as great in the noncauterized as in the cauterized cases.

The diagnoses for the entire series are listed in Table III and represent pathologic reports in all but the mechanical defects. They are presented with the frequency of their occurrence given in percentages. From the table, it can be seen that the occurrence of fibroids, metritis, malignancies, prolapse, and endometriosis total 100 per cent, and the remainder of the diagnoses listed in some measure contributed to the technical difficulties met with in a series of this sort. The number of patients with inflammation is fairly high, there being salpingitis or tuboovarian abscess in 39.4 per cent. Cervicitis was found in 76 per cent of the patients.

Some authors (Greenhill,[4] Schmitz,[5] Fullerton and Faulkner,[6] and Farrar[7]) emphasize the dangers of appendectomy or removal of the adnexa in addition to hysterectomy. In Greenhill's[4] series, the mortality was eleven times as frequent as when the uterus alone was removed. This has not been true in our experience. We do appendectomy almost routinely. In fact, we start below and do everything that we feel is necessary for the patient's future welfare and to prevent

TABLE III. DIAGNOSES

	NUMBER	PER CENT
Cervicitis	1238	76
Fibroids	849	52
Metritis (Chronic metritis, Fibrosis uteri, Chronic subinvolution)	526	32
Salpingitis	602	36
Tuboovarian Abscess	45	2.7
Ovarian cyst	85	5.2
Cystocele	130	6.7
Rectocele	221	13.5
Prolapse	56	3.5
Endometriosis	148	9
Carcinoma: Cervix	14	0.85
Carcinoma: Fundus	41	2.5
Carcinoma: Ovary	25	1.6
Other malignancies	5	0.3
Dermoids	15	0.9

subsequent operations. Each surgeon must know his own limitations in regard to this policy and every surgeon must be cautious about extra procedures in the handicapped patient. Ovarian tissue is preserved as frequently as possible.

The complications associated with the cases operated upon with the above diagnoses represent fairly satisfactory results. Table IV shows the complications and the frequency of their occurrence. It will be noted that of the few operative complications injury to the urinary bladder occurred twice and ureteral fistula occurred once. There were no known injuries to the bladder or ureters in our own series. Postoperatively wound infections, cystitis, and distention were the chief concerns, and the latter two were rather infrequent.

Out of the 442 subtotal hysterectomies done by the authors, there were 2 deaths. One followed an operation for large myomas with adherent adnexa. She had early distention, rapid pulse, and vomiting, and died of a peritonitis or intestinal obstruction. The other death in this group was in a 68-year-old patient with a carcinomatosis, in whom a palliative procedure was undertaken to relieve pain and bleeding. She died on her sixteenth postoperative day from a hemorrhage of the bowel which originated in a penetrating metastatic lesion in her colon. If we may be allowed to correct our subtotal hysterectomy mortality in view of this case, it would then be 0.23 per cent.

TABLE IV. COMPLICATIONS (INCLUDING DEATHS)

	NUMBER		PER CENT	
	ALL CASES	AUTHORS' CASES	ALL CASES	AUTHORS' CASES
Infected wound (not including sinus from drain)	145	33	8.9	6.4
Cystitis	85	31	5.2	6.0
Ileus	53	6	3.2	1.2
Pelvic abscess	21	2	1.3	0.38
Phlebitis, leg	20	7	1.2	1.3
Peritonitis	12	1	0.73	0.19
Pulmonary embolus	11	1	0.7	0.19
Intestinal obstruction	2	0	0.12	0
Pneumonia	11	2	0.7	0.38
Pelvic thrombophlebitis	4	0	0.25	0
Hemorrhage	3	0	0.18	0
Evisceration	4	1	0.25	0.19
Atelectasis	8	2	0.5	0.38
Injury to bladder	2	0	0.12	0
Injury to ureter	1	0	0.06	0

Further analysis of the deaths of the entire series is contained in Table V. Embolus is the chief cause of death (28.6 per cent), with peritonitis as second offender (21.9 per cent). Shock was the factor in 6 per cent. In Schmitz'[5] series, 25.6 per cent of the deaths were attributed to shock. Fullerton and Faulkner[6] and Mathieu and associates[8] listed shock and hemorrhage as the cause of death in 11.6 per cent and 20 per cent of their fatal cases. In our personal series, there were no deaths from shock or hemorrhage. This may be due to our efforts to anticipate and prevent shock by using blood transfusions early in the operation in handicapped patients, or when a severe operation is expected. We had one death from embolus. There were no cases of postoperative intestinal obstruction. Twenty-five per cent of the deaths were in colored patients, although only 13.5 per cent of all the patients were colored.

In three of the four deaths in our own group of total hysterectomies, the operations were performed for carcinoma of the fundus and the patients all presented serious problems from the standpoint of surgical risk and the local conditions of the pelvic organs. The other patient had a fibroid of the cervix, and she is classified as a cardiac death. Pneumonia and cardiac causes are given for the first three. This represents by far the highest mortality for any six-year period, and it is our high mortality in this group that raises the mortality of total

TABLE V. ANALYSIS OF DEATHS

CAUSE	NUMBER OF DEATHS				PER CENT
	SUPRA-VAGINAL	TOTAL	VAGINAL	TOTALS	
Embolus	7	2	1	10	28.6
Peritonitis	8	0	0	8	21.9
Shock	6	0	0	6	17.1
Cardiac	3	1	0	4	11.4
Pneumonia	1	2	0	3	8.6
Carcinomatosis	2	0	0	2	5.7
Thrombophlebitis	0	0	1	1	2.8
Septicemia	1	0	0	1	2.8

TABLE VI. FIVE PRINCIPAL COMPLAINTS

	NUMBER	PER CENT
Pain or discomfort	1,199	73
Bleeding	914	56
Urinary	387	24
Tumor	266	16
Leucorrhea	621	38

TABLE VII. ADDITIONAL PROCEDURES

	NUMBER		PER CENT	
	ALL CASES	AUTHORS' CASES	ALL CASES	AUTHORS' CASES
Cauterization of cervix	1,344	452	82	88
Amputation of cervix	23	12	1.4	2.3
Appendectomy	726	244	44.2	47.5
Oophorectomy Unilateral	560	193	34.7	37.6
Oophorectomy Bilateral	423	79	25.8	15.4
Salpingectomy Unilateral	355	134	21.6	26.1
Salpingectomy Bilateral	746	218	45.5	42.4
Plastic Anterior	126	43	7.7	8.4
Plastic Posterior	260	82	15.8	16.0
Dilatation and curettage	402	64	24.5	12.4
Drain used	446	184	27.2	35.8
Transfusion	248	76	15.1	14.8

hysterectomy in these two hospitals to 4.31 per cent for this period, for the other surgeons had only 1 death in 59 cases, or 1.7 per cent mortality. In the previous six-year period, we had one death from total hysterectomy.

There were 19 vaginal hysterectomies with no deaths in our personal series. The vaginal hysterectomies were done only for third degree prolapse, and many of these were in quite elderly patients.

ROLE OF INFECTION

Infection plays an important role in the mortality of hysterectomy, total or subtotal. Infection is a factor in the occurrence of phlebitis, embolism. In Greenhill's[4] series, 50.8 per cent of the deaths were due to peritonitis and 13 per cent due to embolism. In Schmitz'[5] series, 46.2 per cent were due to peritonitis and 3.8 per cent to embolism, and in Mathieu's[8] series, 40 per cent were due to peritonitis. Dupertuis and Zollinger[9] attribute 9½ per cent of their deaths to wound infection *(B. welchii)* and 28½ per cent to pulmonary embolism. It is very likely that some of the postoperative pneumonias after hysterectomy are secondary to pelvic infection. Therefore, it is evident that if infection could be much reduced or eliminated the mortality and morbidity of hysterectomy would fall markedly.

Some degree of infection of the cervix is present in the great majority of cases in which hysterectomy is done. Cleansing of the vagina, no matter how meticulous, will not eliminate this infection. Some advocates of total hysterectomy contend that postoperative complications such as pelvic cellulitis, phlebitis, embolism, and peritonitis are more frequent after subtotal hysterectomy as it is usually done than after total hysterectomy. Newell[10] states that this is partially explained by the fact that the infected cervix is cut across in subtotal hysterectomy. Goodall[11] also attributes it to mucosal disease of the cervix, and cites the frequent incidence of secondary hemorrhage and parametritis following trachelorrhaphy and amputation of the cervix as further proof of the danger of cutting and suturing the infected cervix. For many years we have felt that the cervix is the principal source of postoperative infection after hysterectomy and have advocated deep cauterization as the best method of sterilizing the cervix preliminary to hysterectomy.

TECHNIQUE

In 1924 the senior author[12] published the technique of deep cauterization of the cervix, and our method of subtotal hysterectomy was published in 1926.[13] The method consists of single or multiple biopsies of the cervix, dilatation of the cervical canal, cauterization of the canal up to the internal os with Downes cautery blade, and then deep, closely placed radial incisions at the external os to extend beyond and beneath the zone of erosion and infection. The purpose of this procedure is to destroy completely the infected cervical mucosa and glands. The extent and depth of the cauterization depends on the extent of the erosion and cystic condition in the cervix. Each radial cut with the cautery blade varies from ⅛ to ¼ inch in depth. One should aim to cauterize too deeply rather than too superficially. In the subsequent care of the patient, stricture can be disregarded, for when hysterectomy and cauterization are combined, the cervix can be permitted to heal with obliteration of the canal. The serious results of cauterization of the cervix, such as cellulitis, peritonitis, etc., which are stressed by some authors, are due in most instances, we believe, to incomplete cauterization, thereby leaving a zone of infected glands beneath the cauterized tissue. Deep cauterization is preferred because sections of the cervix show that the inflammatory process is frequently deep seated, and that it is necessary to cauterize deeply in order to eliminate it. In practicing deep cauterization, some of the shortcomings of superficial cauterization are disclosed that are not generally known. In cervices that have been cauterized superficially, sections taken immediately afterwards or after healing has taken place, reveal too frequently, that the deep glands have not been destroyed and that they are sealed in by the healing process and extensive cyst formation may result. There are many opportunities to observe this today, as superficial cauterization is done so generally in the offices

of physicians. In reoperating on these patients, it is found that many of the cervices are riddled with cysts that are often not evident until deep incisions with the cautery blade are made, and mucus and mucopus evacuate.

We practice deep cauterization of the cervix followed immediately by laparotomy and subtotal hysterectomy. The supravaginal amputation is made low down near the attachment of the sacrouterine ligaments, usually leaving only a rim of cervix. The incision crosses the cauterized and sterilized cervical canal, coning slightly with the knife so as to be able to approximate noncauterized tissue in suturing the cervix. In this method the cervical mucosa is destroyed, the canal is sterilized, hysterectomy is made safer, and future trouble with the stump is practically eliminated. To cauterize or cone out the cervical canal from within the abdomen is not sufficient, for erosions and cysts of the portio cannot be destroyed in this manner.

Treatment of the cervix with the cautery after hysterectomy, as advocated by some surgeons, robs the technique of hysterectomy of one of its most valuable features, namely, preliminary sterilization of the cervical canal. And furthermore, posthysterectomy cauterization may lead to injury of the bladder or bowel which has been placed over the cervical stump.

Formerly, we cauterized only the cervices that did not seem to be normal. However, it was observed that some cervices, which looked normal at the time of subtotal hysterectomy, were found to be markedly inflamed on later examination. This is probably the result of circulatory changes in a glandular structure which predispose to infection. It may be the explanation for the reports of carcinoma developing in a normal cervix after subtotal hysterectomy, for we doubt if carcinoma ever develops in a really normal cervix. Masson[2] has made the same observation and states, "It is known that cervicitis is a very common sequel to subtotal hysterectomy. In more than 500 cases, cervicitis with leucorrhea was sufficient to require treatment after subtotal hysterectomy. In many of these there was no history of leucorrhea before the body of the uterus was removed."

For the last fifteen years, preliminary to subtotal hysterectomy, we have cauterized practically every cervix whether it appeared normal or not. In some clinics the cervix is cauterized and permitted to heal before subtotal hysterectomy is done. This

TABLE VIII. AGE INCIDENCE

AGE RANGE	ALL CASES	AUTHORS' CASES
15-19	6	3
20-24	30	7
25-29	120	47
30-34	297	96
35-39	381	106
40-44	381	119
45-49	242	69
50-54	98	31
55-59	42	18
60-64	26	9
65-69	12	6
70 and over	5	3

TABLE IX. COMPLICATING CONDITIONS ASIDE FROM OR ASSOCIATED WITH THE OPERATIVE INDICATION

	NUMBER	
	ALL CASES	AUTHORS' CASES
Tuboovarian abscess	45	16
Pyosalpinx-hydrosalpinx	46	6
Adhesions	188	88
Carcinoma—Fundus	41	19
Carcinoma—Ovary	25	8
Carcinoma—Cervix	14	2
Diabetes	18	6
Tuberculosis	14	5

is done to eliminate the danger of peritonitis following cauterization of the cervix and immediate hysterectomy. In our experience, this danger has been greatly exaggerated. In fact, we feel that there is no method other than cauterization at the time of operation that so certainly sterilizes the cervical canal. The cauterized cervix opens into the vaginal canal and the microorganisms that appear later in the slough are saprophytes, and there is less danger of peritonitis than if the infected cervix with its pyogenic organisms is left in place.

For the benign conditions requiring removal of the uterus, we prefer subtotal hysterectomy combined with cauterization of the cervix rather than total hysterectomy, for the following reasons: (1) There is no distortion of the vaginal vault and dyspareunia is thereby prevented. (2) It is a simpler operation and therefore applicable to all cases and adaptable to all hands. (3) The infected cervix is adequately cared for in all cases. (4) We have been able to keep the mortality well below 1 per cent in our own series. (5) The end result is a noninfected, smoothly healed cervix, and no subsequent surgical treatment of the cervical stump for inflammation or newgrowth has been necessary in our series.

DISCUSSION

The advocates of total hysterectomy are correct in maintaining that a subtotal hysterectomy which leaves an infected cervix, or one that becomes infected subsequently, is an incomplete operation. But many of these surgeons do total hysterectomy in *selected* cases, and subtotal hysterectomy in handicapped patients and in technically difficult cases, with the result that in the latter group no treatment of the cervix is carried out, and the patient is left with an infected cervical stump. For the past six years our mortality for subtotal hysterectomy has been below 1 per cent in consecutive, unselected cases and the cervix has been adequately cared for by deep cauterization in all but three cases. There has been no necessity for subsequent treatment of the cervical stump for inflammation or neoplasm. As long as that situation prevails, we see no reason for changing to total hysterectomy. We have grave doubts as to whether we could keep the mortality rate at that level if we applied total hysterectomy routinely to a similar series which includes all of the physically handicapped, the adipose, the inflammatory and the technically difficult cases.

Murphy[15] reports the marked increase in bladder and ureteral injuries and in the incidence of pyelonephritis since the more general adoption of total hysterectomy in the Women's Hospital in New York, even in the hands of experienced operators. The ureteral injuries in his series were 0.24 per cent in subtotal hysterectomy and 1.6 per cent, or 6½ times as many, in total hysterectomy. Acute postoperative pyelonephritis was three times as frequent in total as in subtotal hysterectomy in his series. Leventhal[16] in reporting on ureteral injuries states that the larger proportion of these cases occurred after 1930, when the staff began to perform total hysterectomy more often for conditions which were formerly treated by subtotal hysterectomy.

Fullerton and Faulkner[6] reported a 2½ per cent incidence of peritonitis among the postoperative complications of total hysterectomy. Thirty-three and one-third per cent of the deaths after total hysterectomy reported by Newell and Scrivener[1] were due to peritonitis. Deep cauterization is advisable even if one is contemplating total hysterectomy, for it is the most effective method of sterilizing the cervix which is to be removed through the abdomen. In the instance where a total hysterectomy has been planned, but once inside it is decided to do subtotal hysterectomy, the cervix will have been cared for by this preliminary treatment, and a diseased stump will not be left behind.

We do not imply that cauterization of the cervix is alone responsible for the results of this series. It is only one factor. The other factors are:

1. Careful preoperative estimate of the patient's handicaps and the institution of adequate measures to overcome them, such as blood transfusion, not only in the anemic patients but in those who are less able to withstand operative trauma and loss of blood, especially when a difficult operation is anticipated; blood transfusion started at the beginning of the operation and not after the patient begins to show some degree of shock.

2. An incision large enough to give good exposure so that one can reach down to meet the pathologic conditions rather than to drag them up. We have seen surgeons almost lift the patient from the table in their efforts to bring the uterus above the incision. An alert anesthetist can detect too much traction.

3. Expeditious work in the abdomen commensurate with thorough surgery. In abdominal surgery every minute after the first hour is important so far as the postoperative recovery is concerned.

4. Insertion of a sheet of rubber tissue to cover the raw, oozing surface that cannot be peritonized without too much time and trauma. This is done in order to prevent postoperative obstruction and the formation at times of inflammatory exudate from low grade infection in the blood and serum that will accumulate if no exit is provided.

All of these factors help to lower the mortality but an infected cervix adjacent to a pool of blood or serum in the pelvis increases the danger of complications, and these can be avoided by adequate preliminary care of the cervix.

Up to 1938 the late Dr. R. R. Huggins and the senior author had performed 2,525 subtotal hysterectomies. We know of no case in which cancer developed in the remaining stump in this series, of which 506 were contacted in a follow-up study. There is no doubt in our minds that chronic infection is a causative factor in cancer of the cervix. Meigs[18] and Masson[2] both estimate the incidence of cancer in the cervical stump as 1 per cent. Levin[17] states that 2 per cent of all women, if followed to their death, will develop cancer of the cervix. If these percentages were applied to the original Huggins and Cashman series of 2,525 hysterectomy cases since 1914, there should develop 25 to 50 cancers of the stump. We know of none. In such a series it may be that occasionally an incipient cancer, too small to be even suspected on gross examination, has been destroyed by cauterization in the stage which Schiller designates as the primary or superficial and Martzloff the covert stage of cancer of the cervix. It is our belief and experience that a cervix healed and free of infected mucosa after cauterization is no more liable to develop cancer than the surrounding vaginal mucosa.

Total hysterectomy at the Magee and St. Francis Hospitals is reserved almost entirely for cancer of the fundus, cancer of the adnexa, and the occasional cervical fibroid. Our subtotal operation is almost a total hysterectomy, as only a small portion of the cervix is left behind. In the majority of cases, perhaps, the removal of this small portion would add but little to the technical difficulty. But in the remainder, as in the

adipose patient with deep pelvis, and when shortened sacrouterine ligaments and parametrial tissue limit the mobility of the cervix, the technical difficulties are much increased. It is in this group that unnecessary deaths would occur if total hysterectomy were done in every case where hysterectomy is indicated.

CONCLUSIONS

1. Infection plays a prominent part in deaths from hysterectomy.
2. Chronic cervicitis is a source of infection.
3. Deep cauterization of the cervix, as the first stage in hysterectomy, eliminates this source and reduces the mortality.
4. It is advisable in both total and subtotal hysterectomy.
5. It eliminates future inflammatory trouble with the cervical stump and in our experience prevents carcinoma.
6. Deep cauterization of the cervix followed immediately by subtotal hysterectomy has made total hysterectomy unnecessary for benign conditions of the uterus.

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DISCUSSION

DR. WALTER T. DANNREUTHER, New York, N. Y.—There is little difference in the morbidity and mortality of supravaginal and complete hysterectomy in the hands of experienced operators. I have looked up the records of my last 730 personally performed hysterectomies and found that 654 were supracervical amputations, 65 panhysterectomies, and 11 vaginal hysterectomies. Ten patients died after the supravaginal operations, a mortality of approximately 1.5 per cent. There were no deaths, nor bladder or ureteral injuries, after complete hysterectomy, either abdominal or vaginal, so it is evident that like Cashman and Frank, I am prejudiced in favor of the supravaginal abdominal operation, notwithstanding the zero mortality of the complete operation in my hands. My own reasons for this are because of the marital difficulties and dyspareunia which follow ablation of the cervix. If an inquiry is made of each patient subjected to total hysterectomy, the almost invariable confession of subsequent sexual impairment or unpleasantness becomes a forcible argument in favor of cervical retention. Obviously this premise becomes untenable in the presence of extensive cervical disease or malignant, or potentially malignant, lesions.

Like the authors, I remove the appendix routinely and am convinced that appendectomy introduces no additional risks. I cannot agree with Cashman and Frank that infection constitutes an important hazard in the mortality of hysterectomy, since only one death in my series of cases was due to peritonitis. No one can dispute the fact that a diseased cervical stump predisposes to postoperative morbidity and remains a menace throughout the patient's subsequent life as a

focus of infection, or as a likely site for malignant transformations. With ample time for preoperative attention, the majority of damaged or infected cervices can be converted to a healthy state. If the cervix is to be left, the vaginal surface of the portio must be completely epithelized, and the endocervical canal free from infection and inflammatory products. It, therefore, seems much more logical to restore such a cervix to normal by office treatment before the hysterectomy, rather than simultaneously to create a large slough from the extensive cauterization.

The authors indicate that the choice lies between superficial and deep cauterization, and completely ignore conization with the high tension current, and electrocoagulation with the bipolar electrode. It is my practice to disregard the cervix which has been slightly lacerated but is well healed without erosion, ectropion, or infiltration with scar tissue; to cauterize a lacerated cervix with a moderate degree of ectropion or erosion, but which is free from infection; to excise an infected endocervix with the Hyams electrode and the cutting current, or destroy it by electro-coagulation; and to remove a cervix which has been widely lacerated with deep infiltration of the cicatrix, large bulky cysts, associated infection, and ectropion. When there are irregularly eroded or ulcerated areas in the region of the external os, the choice of treatment lies between total hysterectomy and irradiation, rather than between the various types of hysterectomy.

With correct preoperative diagnostic precautions, discriminating treatment of the cervix, and a proper selection of cases, I doubt that the incidence of subsequent carcinoma of the stump is any higher after supravaginal hysterectomy than it is in women who have never been operated upon. In my 654 cases only one instance of carcinoma of the stump has come to my attention, and this was due to a stupid error on my part.

The authors wisely stress the importance of careful preoperative study and preparation of the patient, the value of preoperative transfusions, adequate operative exposure, expeditious technique, and the protection of raw surfaces in the pelvis. When there are denuded areas that cannot be satisfactorily peritonized, I have used sheets of gutta percha tissue for many years to prevent visceral agglutination. This is less cumbersome than rubber tissue. Cashman and Frank are to be congratulated on their low mortality after supravaginal operations, 0.45 per cent, the lowest that has so far come to my attention.

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—On my own service at the clinic approximately 80 per cent of the operations are total hysterectomy and about 20 per cent are subtotal hysterectomy. Little more difficulty is experienced in the removal of the cervix with the fundus from the abdominal side than is encountered in cutting it off and leaving the cervix in position. I have several principal reasons for doing total hysterectomy. One of these is that by so doing the cervix, as a source of infection, is eliminated. Another reason for the total operation is that by means of it the vaginal vault of the multiparous patient can be reconstructed. Dyspareunia will not occur and a much more nearly perfect anatomic reconstruction will be attained.

It has been established that the cardinal ligament is the only useful one in the maintenance of uterine support. Very little can be done with this ligament when subtotal hysterectomy is performed. My plan in removal of the cervix is to shorten the broad ligament and then to re-attach it to the angles of the vagina, and instead of shortening the vagina, I can actually lengthen it.

DR. JOE V. MEIGS, BOSTON, MASS.—In 1932, from one of the hospitals in Boston, came a report of 3,000 cases of cauterization of the cervix with a very small subsequent incidence of cancer. This report was made to show that cauterization would prevent cancer. I accepted that teaching until I had had two patients of my own who developed carcinoma of the stump, both of whom are now dead and could easily have been saved. Since that time I have done total hysterectomies as a practical routine. It is my opinion that it is the operation of choice and is technically as easy to do as a supravaginal operation. I have had only one case of dyspareunia and have asked all of my patients about this symptom.

DR. A. J. RONGY, NEW YORK, N. Y.—No single surgical procedure is equally applicable in every case. The problem of how to deal with the cervix after a supravaginal hysterectomy has been performed in a multiparous woman, in whom the cervical canal very likely is infected because of old lacerations and scarification, is quite different from the problem the cervix presents in the nulliparous patient, especially the elderly spinster, upon whom a supravaginal hysterectomy has to be performed. When clinically there is no infection of the cervix, especially in the unmarried woman, there is no reason for cauterizing the cervical canal and destroying the glands and its lining. The incidence of cancer of the stump of the cervix is definitely small. The mortality following supravaginal hysterectomy and total hysterectomy in the hands of the expert may not differ much, but in the hands of the average surgeon a supravaginal hysterectomy is much safer for the patient than a total hysterectomy. Surely, the incidence of ureteral injury is practically reduced to a minimum.

In patients with relaxed vaginal vaults, in whom a sagging of the vagina is likely to take place after a supravaginal hysterectomy has been performed, I usually anchor the cervical stump to the anterior parietal peritoneum. That often prevents further sagging of the vaginal vault and occasionally obviates many of the annoyances that take place during sexual intercourse in this group of patients.

DR. WILLIAM H. WEIR, CLEVELAND, OHIO.—In our hospital service, the supravaginal hysterectomies show a higher mortality rate than do the panhysterectomies. The probable explanation of this is that in the more difficult cases, with dense adhesions, abscesses, or other complications, many of the operators, in order to save time, will perform the supravaginal hysterectomy instead of the usual total operation and naturally these complicated cases would show a higher death rate than simpler ones.

We perform a vastly greater number of panhysterectomies than supravaginals and last year we had an unusually lucky series. In a period of thirteen months, 470 consecutive hysterectomies were performed by the visiting and resident staff. No death occurred in this entire series. Of this total, 356 were abdominal panhysterectomies, 65 were supravaginal, and 49 were vaginal.

As far as shortening of the vagina as a result of the panhysterectomy is concerned, it need not occur if one is careful to keep close to the cervix in dividing the vagina and to sacrifice no more vaginal wall than is necessary.

DR. A. D. CAMPBELL, MONTREAL, CANADA.—A cervix that needs to be cauterized should above all others be removed when performing a hysterectomy. Carcinoma in the neglected stump approaches 2 per cent, and it is worthy of note that 80 per cent of these occur where the operation was limited to subtotal hysterectomy for chronic pelvic inflammatory disease. I remove the cervix with the uterus in 70 to 75 per cent of cases, leaving the stump in only the elderly nullipara when removing the uterus for a leiomyoma of the corpus.

In the past seven years following total hysterectomy, our uncorrected death rate including those that died from heart disease, embolism, and progressive malignancy was 1.68 per cent.

DR. CHANNING W. BARRETT, CHICAGO, ILL.—The statistics given in the paper show that these men are in the safe class of operators, but this safety did not come from cauterizing the cervix. If that were true I should have had a great many deaths from peritonitis in subtotal hysterectomies, which I have not had.

There has been too little stress laid upon vaginal hysterectomy. In those cases in which the cervix is badly diseased, either from the standpoint of possible development of carcinoma or a benign condition of the cervix, a vaginal hysterectomy in all cases where it is technically possible is the operation of choice. But if we advocate total hysterectomy from above in all cases, we are going to increase the mortality among the average operators far more than we save from developing carcinoma.

Dr. Miller, of New Orleans, has gone very carefully into the question of stenosis, and he puts deep cauterization as one of the principal causes of stenosis of the

cervix. I doubt if a deep cauterization can be done, whether it is complete or incomplete, without a good deal of stenosis. There are pockets of epithelial growth in the cervix and deep cauterization will not reach and dispose of them.

DR. JAMES W. KENNEDY, PHILADELPHIA, PA.—From the discussions we have just heard, one would be led to think that Dr. Cashman was contrasting the difference in mortality and morbidity of complete removal of the uterus as an abdominal operation, with that of supravaginal amputation of the uterus. The paper is, however, dealing with cauterization of the cervix in order to prevent operative infection from the hysterectomy which was to follow.

I am entirely in accord with the teaching the doctor has advanced. I would as soon undertake to perform a hysterectomy from above or below, without washing my hands, as I would attempt to operate without thoroughly cauterizing the cervix and making a very thorough toilet of the vaginal canal, which is accomplished by soap and scrubbing brush.

Cauterization of the cervix after supravaginal hysterectomy has been performed is a step of great value as a prophylaxis against occurrence of malignancy of the remaining cervix. The teaching is of particular worth to those operators who cannot perform a panhysterectomy with as low mortality as that of supravaginal amputation of the uterus.

Although today the teaching is in favor of a greater number of complete operations, there is a difference in the mortality of a complete hysterectomy as compared with supravaginal amputation of the uterus, in favor of the latter, and especially so in the very fleshy woman with cardiorenal symptoms. There is then a broad field of usefulness for the points brought out in Dr. Cashman's discussion.

Reference has been made to shortening or distortion of the vaginal canal following complete hysterectomy when performed either as a vaginal or abdominal operation by the ligature method. Over 95 per cent of the hysterectomies performed in the Joseph Price Hospital are executed as vaginal hysterectomies by the clamp method, and we find in practically all cases the vaginal canal is lengthened. The only exception to such results occurs in those patients where we have removed an extensive amount of the vaginal fornix for malignancy of the cervix.

DR. MORTIMER N. HYAMS, NEW YORK, N. Y.—Far too frequently when reference is made to chronic endocervicitis, the type or degree is not considered. Based on Mathews' classification, a first-degree involvement would not necessitate the same therapeutic measures as would a fourth. While cauterization of the cervix has advantages in certain forms of cervical pathology, it cannot be considered a cure-all for every form of chronic infection. I believe that the age of the patient and the extent of the pathology in the cervix must be the index for the method of attack.

DR. CASHMAN (closing).—Deep cauterization is our method of treating these cases, but we are in favor of any method that cleans up the cervix in treating cases of cervicitis. A stricture is not a factor when you are doing a hysterectomy.

A recent patient of mine, who had been cauterized twelve years ago, was found to have a cervix honeycombed with cysts, but this was not the result of the kind of cauterization we are talking about. If you are going to deal with the cervix properly you must destroy every bit of epithelium. If cauterization is done completely at the time of operation, no further cauterization is necessary.

We have watched these patients in whom we did not cauterize the normal cervix at the time of hysterectomy, and they have come back with an inflamed cervix later on. In many of these there was no history of leucorrhea. Up to 1938, Dr. Huggins and I did 2,500 subtotal hysterectomies with cauterization of the cervix and with no known carcinoma of the stump in that number. We made a follow-up of 506 of the patients.

THE EFFECTS OF ANALGESIA ON THE NEWBORN INFANT*

C. O. McCormick, M.D., Indianapolis, Ind.

PERHAPS no single issue divides obstetricians so much as that relating to the use of analgesia. Some do not use it, and criticize it severely; others use it and praise it loudly. Nevertheless, analgesia is indispensable in the modern conduct of labor, and is here to stay.

Among the important reasons against its general acceptance is its purported ill-effect upon the infant. Even strong advocates of childbirth relief share this misgiving to some extent, conceding that in sedating and narcotizing the laboring mother they routinely risk jeopardizing the newborn infant by inducing as a rule at least a brief apnea, and occasionally a marked, sometimes alarming asphyxia.

Certainly, concern in behalf of newborn infants delivered under the influence of maternal analgesia has been strongly bolstered by the report of Schreiber,[1] indicating remote cerebral damage where analgesics are given in excess of pharmacologic doses.

Though long since granted analgesia aids the mother by sparing her mental and physical shock and exhaustion, because of the more or less general presageful feeling mentioned above, there has been but little or no surmise that analgesia might benefit the infant as well as the mother. Gratifyingly enough, recent studies by independent investigators indicate this to be true.

The purpose of this presentation is twofold: First, to show the effects of various analgesic agents in common usage as they reflect upon the initial respiration and mortality of the newborn; and second, to stress the safety of certain popular present-day methods of relief, and compare their enhancements upon the infant. In major part, this will be attempted by correlating the outstanding findings of several investigators.

Regardless of what enhancing effects may result upon the infant, all forms of childbirth relief, except those of local infiltration, do have a large and variable incidence of at least one ill-effect, namely, depression of the respiratory center. This was well illustrated by the study of Irving and his co-workers,[2] covering eight types of analgesia (Fig. 1).

In the most favorable instance apnea occurred in 35 per cent of the cases. This is in marked contrast to the 2 per cent incidence found among cases without relief medication. In the extreme instance, the percentage of apnea rises to 67 per cent.

It is observed that pentobarbital and rectal ether, the modified Gwathmey method, holds the most favorable position. The pentobarbital-scopolamine method, probably the one most generally used today, holds a close second position.

*Read at the Fifty-Third Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., September 26 to 28, 1940.

It is of interest to note that in comparing the effects of sodium amytal and pentobarbital, when each is used separately with the same agent, there is a small but notable increase of apnea in the instance of sodium amytal. When used with scopolamine, the increase was found to be 2 per cent; when used with rectal ether, 6 per cent. Fifty per cent of pentobarbital-paraldehyde babies showed apnea, while fully two-thirds of pantopon-scopolamine patients were apneic.

A further study of analgesics and their effects upon the respiration of the newborn infant are furnished in an unpublished report by Dr. Carl P. Huber of our clinic at Indiana University (Table I).

In this series of 656 cases, comparative studies were made of cyclopal and carbromal; cyclopal, carbromal, and rectal ether; sodium pentobarbital; and sodium pentobarbital and rectal ether.

It is noted that the percentages of immediate spontaneous respiration of the various groups are quite comparable, ranging from 65.6 to 77.4 per cent, while the average for the groups was 73.6 per cent. The average "immediate" and "delayed spontaneous" totaled 85 per cent. Twenty-five per cent of the infants were born apneic.

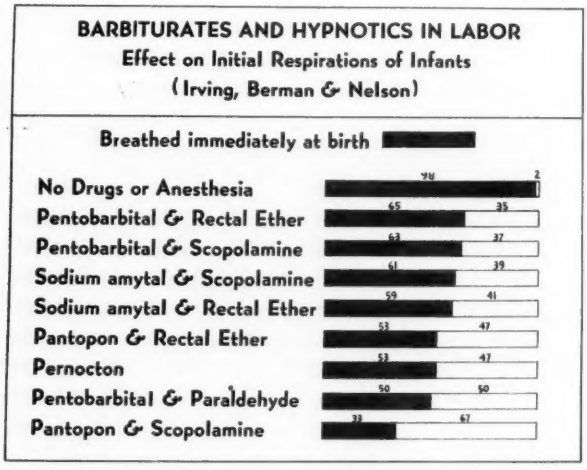

Fig. 1.

TABLE I. THE EFFECT OF CERTAIN ANALGESICS ON INITIAL RESPIRATION OF NEWBORNS
HUBER: OBSTETRICAL DEPARTMENT, INDIANA UNIVERSITY

ANALGESICS	NUMBER OF CASES	SPONTANEOUS AND IMMEDIATE	DELAYED, NO RESUSCITATION	RESUSCITATION	STILLBIRTH RATE
Cyclopal	115	77.4	8.7	11.3	2.6
Cyclopal and rectal ether	96	65.6	17.8	13.5	3.1
Cyclopal and carbromal	87	75.8	12.6	11.5	0.0
Cyclopal, carbromal and rectal ether	111	74.8	9.0	15.3	0.9
Sodium pentobarbital	136	70.6	13.9	12.5	2.9
Sodium pentobarbital and rectal ether	111	77.4	10.8	10.8	0.9
Total	656	Av. 73.6	12.0	12.5	1.8

Fortunately apnea appears to have no serious ill-effect upon the life of newborn infants. Presumably this is partially due to the normal anoxemic state before birth. The gross stillbirth rate of Irving's group was 0.93 per cent, that of Huber's, 1.83 per cent.

Any bona fide effect of an analgesic agent should reflect in the stillbirth and neonatal mortality rates. Clifford and Irving,[3] by checking into the stillbirth and neonatal losses at the Boston Lying-in Hospital over a five-year period, preceding the use of barbiturates and a like period following the introduction of barbiturate analgesia, discovered that both the stillbirth and neonatal mortality rates decreased during the barbiturate period (Fig. 2).

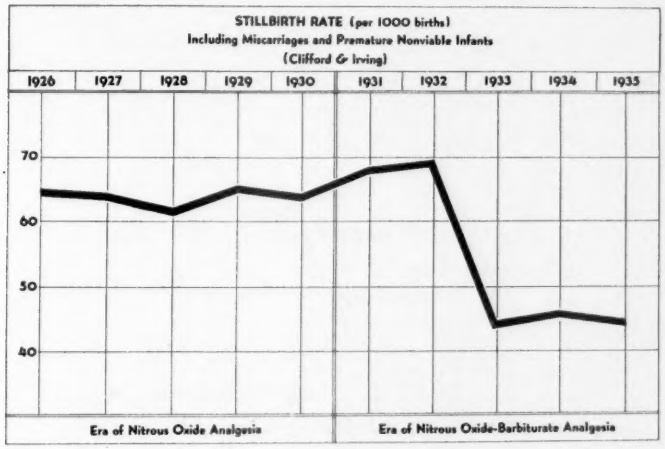

Fig. 2.

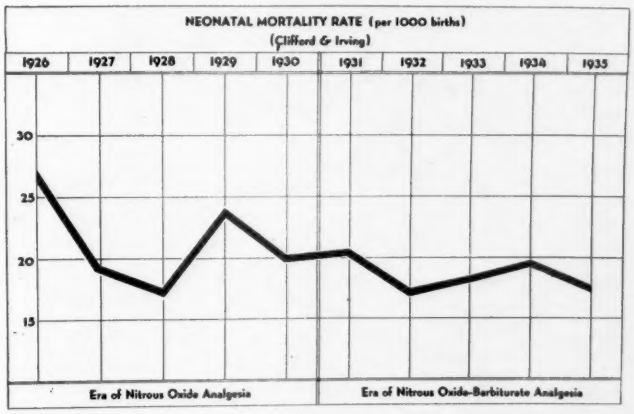

Fig. 3.

The stillbirth rate fell from 65 per 1,000 births during the prebarbiturate era to 56 in the following five years, and the neonatal loss dropped from 22 to 19 per 1,000 births (Fig. 3).

Among the first studies to show benefit from maternal analgesia or anesthesia to the newborn infant was that of Cole,[4] in which he analyzed the effect of ether anesthesia (Fig. 4).

Babies born to unanesthetized mothers experienced a maximum loss of 5.53 per cent of the birth weight. Those born to mothers, who had less than fifteen minutes of inhalation ether, had a maximum loss of 5.2 per cent. Where the ether

inhalation lasted from fifteen to sixty minutes, the weight loss was 5 per cent; and where ether was employed over one hour, the loss was only 4 per cent of the birth weight.

Also, babies born to etherized mothers regained their birth weight more rapidly than those born to mothers receiving no anesthesia. Where the mothers had no medication, the average baby's weight was still 2.37 per cent below birth weight on the eighth day; while the average weight of those babies born to mothers having ether over one hour exceeded the birth weight 0.58 per cent on the eighth day.

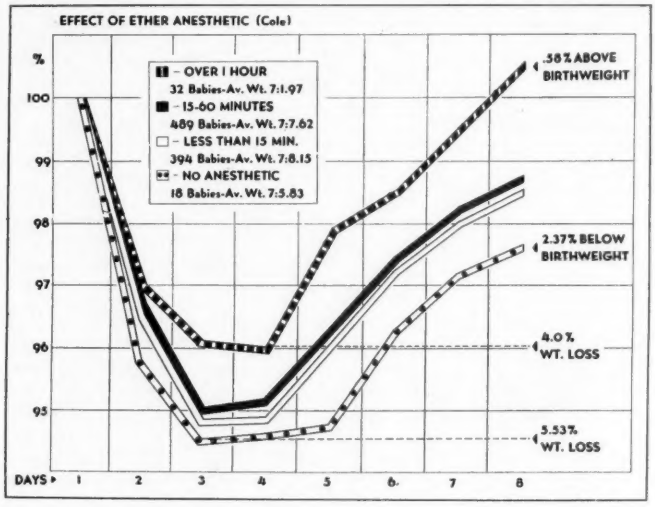

Fig. 4.

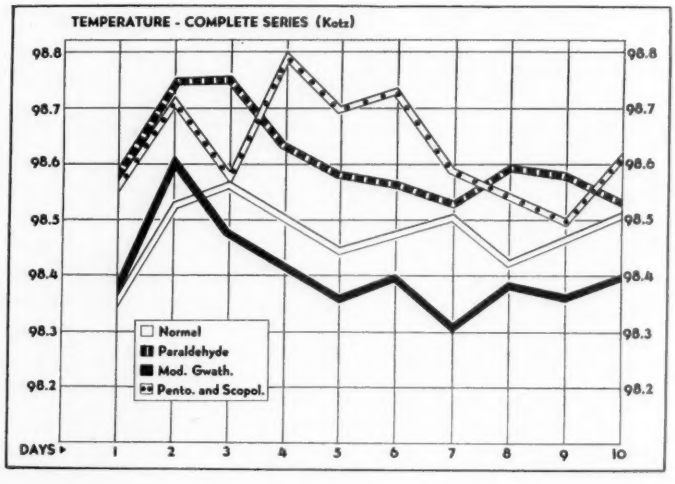

Fig. 5.

Cole attributes this favorable showing to the reduction of birth shock in the baby, and rightfully points out that the so-called "physiologic weight loss" may be more than just physiologic, and perhaps is a direct index of the amount of shock.

Early neonatal welfare is indicated by at least three factors: the daily temperature curve, the amount of weight loss, and the rate of weight loss recovery.

Kotz and Kaufman[5] in their outstanding work, based upon these three standards, have well proved from the viewpoint of the infant's welfare the justification of wisely used analgesia. His study, covering 700 analgized delivery cases, was directed upon the analgesic effect on the infant. The temperature, weight loss, and weight gain during the first ten days of life were closely followed. In addition he ran a control series of 100 babies born to mothers receiving no medication. *All babies were handled under similar nursing care.*

The group of 700 analgized mothers consisted of 500 delivered under the influence of paraldehyde, 100 under pentobarbital-scopolamine, and the remaining 100 under the modified Gwathmey method. His work further included a comparative analysis of these three commonly used forms of relief as to their respective effect upon the infant.

The observed temperatures in each of the three methods studied and that of the babies born to unmedicated mothers are shown in Fig. 5.

It is noted that the temperature of the paraldehyde group and that of the modified Gwathmey method run quite parallel to normal, the former slightly above and the latter slightly below. In contrast, that of the pentobarbital-scopolamine series diverges, running higher, especially on the third, fourth, and fifth days.

It is to be observed in Table II that both the paraldehyde and modified Gwathmey methods present a more favorable showing than the normal, and of the two methods, the paraldehyde is the slightly more favorable.

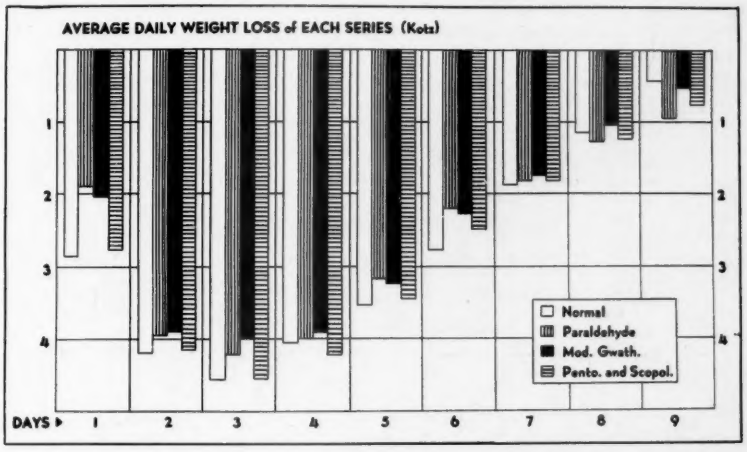

Fig. 6.

TABLE II. PERCENTAGE OF BABIES WITH TEMPERATURES OVER 100° F. (KOTZ)

	DAY POST PARTUM									
	1ST	2ND	3RD	4TH	5TH	6TH	7TH	8TH	9TH	10TH
Normal	2	4	4	5	2	2	1	0	1	0
Paraldehyde	1.4	2.2	3.6	1.6	1.8	1.4	1	0.4	0.2	0.4
Modified Gwathmey	1	4	2	4	1	1	1	1	1	1
Pentobarbital and scopolamine	1	8.3	4.1	8.3	8.3	8.3	2	4.1	4.1	1

Here again, the pentobarbital-scopolamine method stands out in unfavorable contrast. On the second, fourth, fifth, and sixth days, 8.3 per cent of the patients ran a temperature of over 100° F., from two to eight times that of either of the other two analgesic groups.

Further studies compare the average daily weight loss of each of the methods of relief and that of the normal group (Fig. 6).

It is noted that the results of the paraldehyde and modified Gwathmey methods show more favorably than those of the normal and pentobarbital-scopolamine groups throughout the first six days. Also, the greatest maximum weight loss occurs among babies born to mothers having no analgesia and to those having pentobarbital-scopolamine. It is further observed that babies born under the influence of the modified Gwathmey method return to normal weight more rapidly than those delivered under either paraldehyde or pentobarbital-scopolamine.

In comparing the maximum weight loss of each of the three forms of relief and that of the normal group (Table III), it is observed that the greatest loss occurs among babies born to mothers having no medication.

TABLE III. AVERAGE TOTAL WEIGHT LOSS ON THIRD DAY (KOTZ)

	OZ.
Control (100 babies)	4.7
Pentobarbital and scopolamine (99 babies)	4.6
Paraldehyde (498 babies)	4.5
Modified Gwathmey (98 babies)	4.1

Those born under either the pentobarbital-scopolamine or paraldehyde methods suffer an average total weight loss almost equal to that of the normal group, while the babies born under the modified Gwathmey method are favored by a definitely less weight loss. The average of the first three groups is 4.6 ounces, that of the latter, 4.1 ounces.

Another study affords a comparison of the results of various types of deliveries as performed upon mothers having no analgesia and those having one of the three forms, paraldehyde, modified Gwathmey, and pentobarbital-scopolamine (Table IV). This study is important because that which alters the type of delivery may reflect upon the welfare of the infant.

TABLE IV. TYPES OF DELIVERY (KOTZ)

	NORMAL %	PARALDEHYDE %	MODIFIED GWATHMEY %	PENTOBARBITAL AND SCOPOLAMINE %
Low Forcep	2	81.4	21	87.5
Midforcep	1	10.3	3	4.0
Breech	3	3.3	5	8.0
Version Extraction	0	0.5	1	0
Spontaneous	94	4.5	70	4.0

The low percentage of patients delivered by low forceps in the normal group is quite striking compared with the high rate in either of the analgesia groups. However, the low incidence of employment of low forceps among the modified

TABLE V. EFFECT OF SEDATIVES AND ANESTHESIA ON THE MORTALITY OF PREMATURE INFANTS

2,500 GRAMS OR LESS (GRIER)

	TOTAL CASES	CASES LIVED	CASES DIED	MORTALITY %
No sedative or anesthesia	18	10	8	44
Local infiltration	21	17	4	19
Sedative only	19	14	5	26
Anesthetic only	236	172	64	27
Sedative and anesthesia	155	125	30	19
Not stated	4	2	2	50
Total	453	340	113	25 Av. Gr.

Gwathmey group compares very favorably with the much higher rates found in the paraldehyde and pentobarbital-scopolamine series. Also, the 70 per cent incidence of spontaneous deliveries in the modified Gwathmey series is noteworthy when contrasted with the 4.5 per cent and the 4 per cent incidence noted, respectively, among the paraldehyde and pentobarbital-scopolamine groups.

In summarizing briefly this study of Kotz, it is indicated, at least, that the two forms of obstetric analgesia, paraldehyde and modified Gwathmey methods, are favorable to the infant. Further, that of these two, the modified Gwathmey appears to be the more favorable. Regarding the pentobarbital-scopolamine method, the data presented would indicate that its effect upon the baby is adverse.

A discussion such as this properly includes special reference to the effect of sedation and anesthesia upon the life of premature infants. In this instance interest is prompted not solely in behalf of life-saving, but to take advantage of their susceptibility to reaction.

One such study has been made by Grier and Lussky[6] who analyzed the mortality effects of sedatives and anesthesia in a survey of 453 premature infants, weighing 2,500 Gm. or less (Table V).

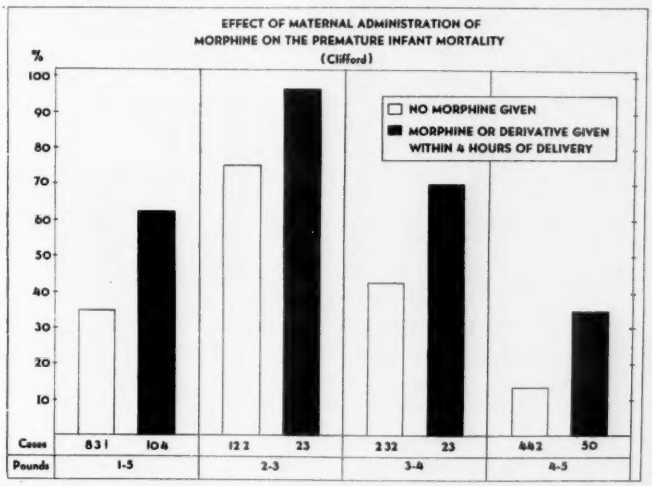

Fig. 7.

Certain observations are noteworthy. For example, the mortality rate among those delivered under both sedation and anesthesia, numbering 155 or a full third of the group, was only 19 per cent. This rate was the same as that for infants whose mothers had only local infiltration, and was less than the average gross mortality rate of 25 per cent. Also, the rates of the two groups, "sedatives only" and "anesthesia only" were, respectively, 26 and 27 per cent, closely approximating the gross mortality rate. The small number of 18 patients, in whom no medication was administered, presented a rate of 44 per cent, the highest of all.

Admittedly this study is not one of close analysis, and no doubt were some of its data broken down deductions might not be so favorable. Yet the statement remains, that the mortality rate among 155 premature infants weighing 2,500 Gm. or less born to sedated and anesthetized mothers was only 19 per cent.

A more pertinent investigation, particularly as relates to the use of opiates, is that of Clifford,[7] which shows the striking effect upon premature infant life of morphine and its derivatives when administered within four hours of birth (Fig. 7).

The mortality rate of infants having received morphine was twice that of those born to mothers not receiving the drug.

Clifford's study further reveals that the mortality rate of prematures born to mothers receiving morphine varies in direct relation to the amount of the drug given (Fig. 8).

These findings strongly substantiate the long commonly held opinion that opium derivatives, when administered within a few hours of birth, render a deleterious effect upon the infant.

Owing to the popular use of nitrous oxide-oxygen in maternal analgesia and anesthesia, special reference should be made to its action upon the newborn.

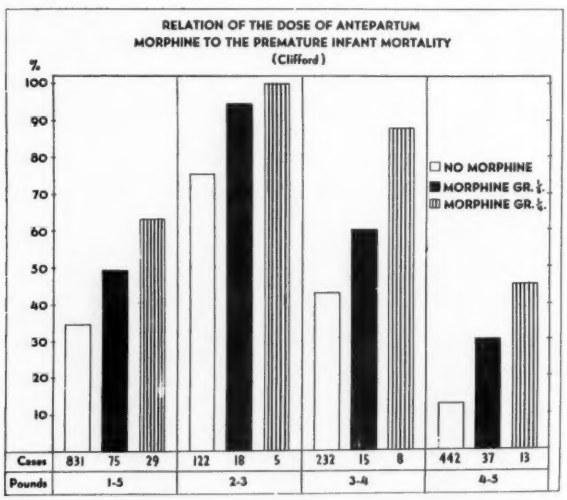

Fig. 8.

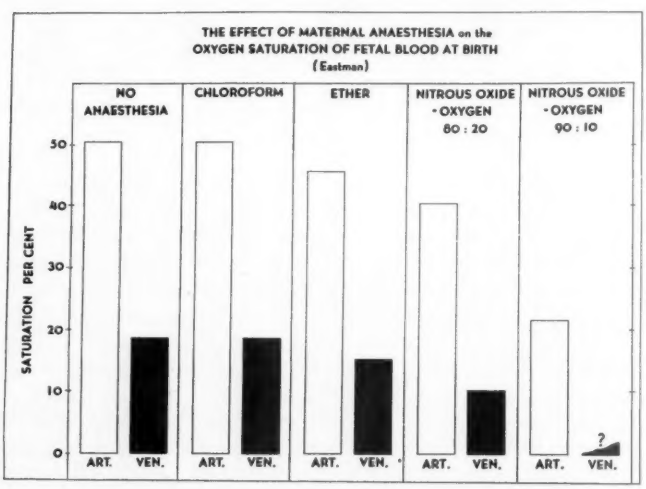

Fig. 9.

Eastman[8] has demonstrated its production of fetal anoxemia (Fig. 9), and points out the risk of profound asphyxia when concentrations higher than 85:15 are employed. His study showed that when concentrations of 90:10 or stronger were used over a period exceeding five minutes one-third of the babies suffer a marked anoxemia, and occasionally profound asphyxia results.

From the viewpoint of anoxemia produced, cyclopropane with the customarily high percentage of oxygen is a more practical analgesic agent than nitrous oxide-oxygen.

More substantial information relative to the influence of maternal analgesia upon the life of the newborn may be gained by comparing the average stillbirth rate of several series of infants born to analgized mothers with that of the stillbirth rate in general. The compilation at hand (Table VI), presents the average rate of the former group to be 1.87 per cent, while that of the general group is conservatively stated by most authors to be in excess of 4 per cent.

TABLE VI. STILLBIRTH RATES OF INFANTS BORN TO ANALGIZED MOTHERS

SERIES	NUMBER OF MOTHERS	NUMBER OF STILLBIRTHS (GROSS)	STILLBIRTH RATE % UNCORRECTED
Galloway et al.[9]	1,415	31	2.19
Huber[10]	656	12	1.83
Irving et al.[2]	860	7	0.93
Kotz and Kaufman[5]	700	14	2.00
Krebs et al.[11]	3,720	60	1.61
Lewis[12]	500	15	3.00
McCormick[13]	1,929	45	2.33*
Whitefield[14]	744	13	1.76
Total	10,524	197	1.87 Av. Gross

*Includes premature nonviable infants, antenatal deaths, and stillbirths of all operative cases.

This favorable showing by no means should be fully accredited to the use of analgesia, since as a whole patients who receive analgesia also receive better obstetric care, both during the prenatal period and at the time of delivery. On the other hand from the data presented, it is seemingly true that many varieties of popular analgesia do not react adversely upon the life of the newborn infant.

CONCLUSIONS

1. The high degree of general safety and security for the newborn as revealed by a correlated study of the many modern varieties of childbirth relief is reassuring.

2. Opiates are probably the only analgesics that may materially affect the infant adversely, and may be particularly hazardous in cases of prematurity.

3. Based upon augmenting the welfare of the newborn, the three standard analgesic methods, modified Gwathmey, paraldehyde, and pentobarbital-scopolamine, appear to rate in the order named.

4. By eliminating the "physiologic weight loss" (birth shock) and enhancing the fetal and neonatal welfare, wisely used obstetric analgesia is no longer a privilege but a prerequisite of better obstetrics.

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DISCUSSION

DR. EMMETT D. COLVIN, Atlanta, Ga.—Schreiber has confronted the obstetricians with an important problem, for he has clearly shown that a relationship between asphyxia at birth and serious degenerative brain changes exists. He concludes that drugs, administered for the relief of maternal pain during labor, may be the causative factor.

He has pointed out a danger which obstetricians thought did not exist. At least the general feeling has been that babies with simple apnea, once resuscitated were safe and developed along a normal course. Of course, Schreiber did not attempt to determine the exact role played by dystocia, operative interference, oxytocics, and general anesthesia. It is therefore, unfair to condemn amnesia and analgesia methods without evaluating these factors.

In discussing this subject, one must constantly keep in mind the influence of drugs upon the increased incidence of uterine inertia and operative termination of labor. Analgesic drugs, by creating the necessity for operative delivery and the accompanying increased incidence of intracranial injury, are responsible indirectly for the asphyxia so frequently encountered among injured babies.

Since 1932, Bartholomew and I have employed 3 gr. of nembutal (pentobarbital sodium) and 6 drams of paraldehyde, by mouth, in the conduct of 2,363 private cases. When necessary, supplementary small doses of paraldehyde were used as indicated in order to secure sleep. In an occasional case a small dose of morphine and scopolamine preceded the initial dose of paraldehyde. The effect of the drug itself upon the mother or child has not caused apprehension, on the part of the attendants, in a single case among the 2,363 deliveries.

An analysis of our series yielded the following data: complete amnesia in 92 per cent; partial amnesia in 6 per cent and failure in 2 per cent; troublesome restlessness in 7 per cent; spontaneous delivery in 80 per cent; average duration of labor in nulliparas, thirteen hours and eighteen minutes; in multiparas eight hours and fifty minutes; and a corrected fetal mortality of 1 per cent.

The incidence of apnea among term babies was 9 per cent. This apnea seemed to be due to a state of drowsiness rather than to a respiratory depression. We have not noted a detrimental neonatal effect. Clearing of the air passages, followed by spanking or gentle mouth-to-mouth inflation of the lungs promptly established good respiration and crying. The apnea was prolonged if morphine and scopolamine preceded the paraldehyde. We found that with premature infants the apnea was exaggerated, and sluggishness predisposed to atelectasis. Aside from drowsiness, in the first six to eight hours after birth, term babies showed no difference in nursing, temperature curve, gain in weight, and behavior from babies delivered without the aid of paraldehyde.

We believe that paraldehyde in combination with a small dose of pentobarbital sodium is a safe method to be employed in childbirth, and, in the hands of capable obstetricians, should not result in greater danger to the mother or infant than drop ether.

DR. W. WAYNE BABCOCK, Philadelphia, Pa.—Dr. McCormick's paper brings attention to the very important question: What percentage of "stillbirths" and of deaths in early infancy result from narcotics and anesthetics given to the mother during labor? I question if this danger ever has been overestimated.

Anesthetics and narcotics commonly produce anoxemia, which our expert neuropathologists have shown may greatly damage the brain. Even cyclopropane, pre-

scribed for the high percentage of oxygen with which it may be used, has caused permanent cerebral damage or death. I know of several deaths occuring at the Philadelphia General Hospital several days after operation from this cause. These deaths had been attributed to other conditions until the histopathology of the brain was revealed.

The anoxemia incident to the administration of general anesthetics and narcotics has in my experience been the most important single factor in the mortality following operations upon young babies. As a result we use only local anesthetics for the newborn infants.

Ravdin and his group have shown that even the serious degenerative change occurring in the liver under chloroform anesthesia may be prevented by the associated use of oxygen. The difficulty in preventing some degree of cyanosis renders nitrous oxide-oxygen and even ethylene anesthesias dangerous for prolonged administration. Doubtless careful postoperative studies would show more frequent cerebral damage from anoxemia in the living than is generally recognized. Oxygen should not be withheld if there is any degree of prolonged anoxemia in either infant or adult.

DR. WARD F. SEELEY, DETROIT, MICH.—In Detroit where the work of Schreiber and Cole was done we have been very sensitive to the question of anoxia. We are not so much concerned with a high primary fetal mortality after the use of analgesia, for needless to say if this occurred we would discontinue its use. We are concerned, however, with the "devastation areas" in the brain which manifest themselves much later and can be demonstrated at autopsy by a competent neuropathologist.

The burden of proof would seem to be with us. We have to show that we do not get babies with such devastated brain areas with properly controlled analgesia. This is difficult because in many instances the results of anoxia do not manifest themselves at once, and it is only when the child comes under the care of the pediatrician or neurosurgeon, with mental defect, that the true state of affairs is recognized.

DR. G. D. ROYSTON, ST. LOUIS, MO.—There are two points in this presentation I should like to emphasize: First, apnea is often associated with delay of the fetal head at the vulval ring, regardless of the employment of analgesia. Second, opium in any form is a respiratory depressant. Laboratory studies in the Washington University Clinic have shown that it depresses the respiratory system and constricts the bronchioles. These studies, together with a clinical experience of more than 20,000 deliveries, also show that hyoscine or scopolamine in moderate dosage exerts no effect upon either heart or respiration of the newborn.

Fetal damage seems to depend upon the depth and extent of the anoxemia, whether caused by injections or the inhalations.

In the chart shown by Dr. McCormick it is interesting to note that 3,720 cases reported by my associate, Dr. Krebs, showed an uncorrected fetal mortality of 1.61 per cent. Krebs reported the largest number of cases and his fetal mortality was the lowest in this chart, being outranked only by Irving who reported a smaller number of cases.

There are many variations of analgesic administration. My personal custom is to wait until satisfied that labor is definitely in progress, then to give by mouth 3 gr. of nembutal and 1 c.c. of hyoscine hydrobromide intramuscularly. The nembutal is never repeated, but forty-five minutes after the first dose a second injection of 1 c.c. of hyoscine is given, followed forty-five minutes later by a third injection of 0.5 c.c. After this third dose 0.5 c.c. of hyoscine is injected every one and one-half to two hours until the patient is delivered. This analgesia for more than twenty-five years has been safe in our hands, and what test is better than a clinical experience of more than 20,000 cases? It enables us to limit certain major obstetric procedures to none or to those of minor import.

DR. FRED L. ADAIR, CHICAGO, ILL.—We have been very much interested in the problem of determining the causes of stillbirths and neonatal deaths, and as far as the autopsies are concerned, I would point out that we find in a considerable

percentage of these babies that we cannot determine the cause of death. There are thus other than the morphologic factors concerned in the death of these babies who die before or soon after they are born.

So far as Dr. Schreiber's experimental work is concerned, it tallies with our clinical observations that the barbiturates are very depressing. I would also emphasize that the effect of these drugs is apparently not a direct effect on the fetus so much as on the mechanism of labor and the establishment of respiration in the newborn. That and the anoxemia that accompanies it are the real factors. Consequently not only the depth but the duration of the anoxemia is extremely important, and we should realize the great importance of promptly securing oxygen for the newborn baby.

In the statistics on weight loss there was no base established to show the original weight of the infants. We all know that the heavier infant will lose more weight in actual ounces than the smaller infant. In these tables there was nothing that showed what the weight was at birth, nor any comparison between the different groups as to their actual weight.

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—I was in the clinic of a very well-known European obstetrician some years ago and brought up this subject of labor analgesia. He said that since so many articles had appeared in popular American magazines, all of his patients demanded that they be given pain relief, and that he had devised something which was very effectual. He gave them a small two-ounce bottle and told them to take half the contents when the pain began and, in another hour or two to take the other half. When they awakened they asked for more. He said it was merely brandy, and they were half "tight" when they were delivered, and consequently remembered little of what had taken place. In his opinion the procedure was effective and harmless and did not hurt the baby.

DR. McCORMICK (closing).—Dr. Babcock properly directs attention to a broader view of our subject by inquiring as to neonatal deaths following the use of analgesia. Of the various current reports studied, only one afforded this information. Krebs and his co-workers in a series of 3,720 cases recorded 36 infant deaths, while the mothers remained in the hospital, an incidence of 0.97 per cent. In a series of 3,446 infants born to unanalgized mothers, they found 48 such infant deaths, or an incidence of 1.39 per cent.

I might add that in four major maternities in Indianapolis where analgesia, for the most part the modified Gwathmey method, has been used for the past ten years in an excess of 30,000 cases, vital statistics do not reveal an increase in either stillbirths or neonatal deaths.

Schreiber's work was based upon unpharmacologic dosage of certain analgesics, and although a most important and invaluable study, it does not properly apply to intelligently used analgesia, such as implied in our presentation.

I wonder if it is Dr. Adair's impression that there is a greater incidence of unexplained stillbirths and neonatal deaths since the advent of modern analgesia. No doubt the massive doses of barbiturates, such as 9 to more than 20 gr. of pentobarbital as employed by some, may produce undesirable anoxemia by both interfering with mechanism of labor and by hindering the establishment of respiration. We avoid this danger in our clinic by using small divided doses, 1½ to 4½ gr., in conjunction with rectal ether, a patient rarely receiving more than a total of 7½ gr.

Dr. Adair's assertion that the statistics presented relative to weight loss were misconstrued seems not to be fully correct. In the first place, granted the larger the baby the greater the weight loss and the smaller the baby the less the weight loss, the importance of such a variation diminishes as the size of the series increases. In that the series cited were reasonably large, and the infants were given similar nursery care, it would appear that any effect registering consistently would be practically significant. In the instance of Fig. 4, such an error was offset by expressing the weight loss in percentage of birth weight.

A REPORT ON A SERIES OF COMPLETE TEARS OF THE PERINEUM WITH EXTENSION UP THE POSTERIOR VAGINAL WALL, REPAIRED BY THE VAGINAL FLAP METHOD*

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(From the Department of Obstetrics and Gynecology, University of Wisconsin Medical School)

THE vaginal flap operation for chronic complete tears of the sphincter of the anus with extension into the rectum and up the posterior vaginal wall is not a new procedure. As early as 1882 Warren described the vaginal flap operation in his monumental presentation. Two years later Ristine added an important publication. Since these early contributions several writers have published articles upon this subject, notably Phaneuf,[5] Miller,[3] Farrar,[2] and others. To those interested in a most complete bibliography and historical background upon this subject, a reference may be made to the important article of Norman F. Miller entitled "The Surgical Treatment of Complete Perineal Tears."[3]

It is the essayist's conviction that too few physicians are familiar with the vaginal flap technique and its excellent results, and he does not exclude obstetricians and gynecologists. In addition, most of my patients have come from the general practitioners of medicine who are the larger group practicing obstetrics in this country.

I am reporting a series of 39 patients upon whom I have operated and have been responsible for their complete supervision. The operation to be described in this series differs from the original Warren technique as noted in the vaginal flap dissection, and the repairing of the triangular ligament and the pelvic floor.

In general, it is true that most operators differ slightly in the detailed technique of the vaginal flap operation and the restoration of the supportive structures; however, they are fundamentally accomplishing the same results as to reparation and successful functioning end results. Miller has so aptly pointed out that the success of any plastic operation is dependent upon a good blood supply, absence of infection, and the avoidance of suture tension. Phaneuf gives warning and stresses not only a meticulous technique but emphasizes the necessity of a careful preoperative and postoperative treatment under the immediate supervision of the operator.

TECHNIQUE

It is important to do a reparative operation several months after confinement when involution is complete and at a time immediately following the menses.

The preoperative preparation of a patient is most important. A low residue diet should be given three to four days preceding the operation. An ounce of castor oil is given daily three to four days prior to the operation. A soapsuds

*Read at the Fifty-Third Annual Meeting of the American Association of Obstetricians and Gynecologists, Excelsior Springs, Missouri, September 26 to 28, 1940.

enema is given the day before the operation; and the morning of the operation a high cleansing enema is given.

The technique of the vaginal flap operation and restoration of the pelvic supportive structures are shown in illustrations taken at operation and reproduced by an artist.

Fig. 1 shows the laceration in situ, and configuration of the pelvic structures. In addition, the retracting of the posterior vaginal wall is illustrated with the outlining of the vaginal flap which begins outside the dimples formed by the retracted sphincter and continues as outlined. Finally, the flap is shown dissected in close

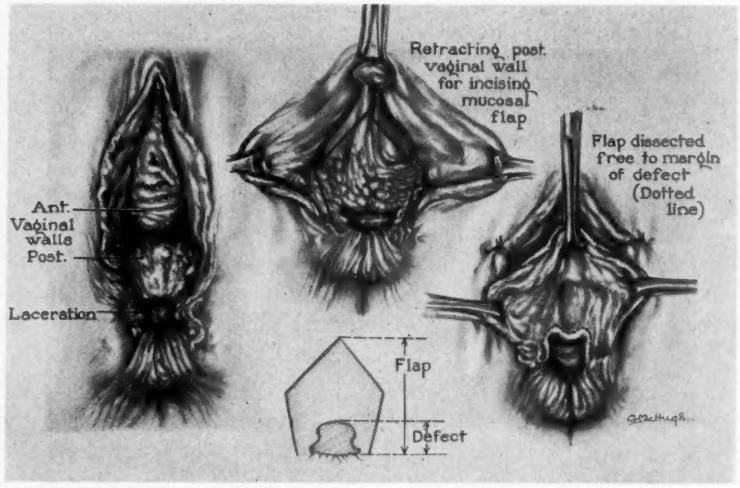

Fig. 1.

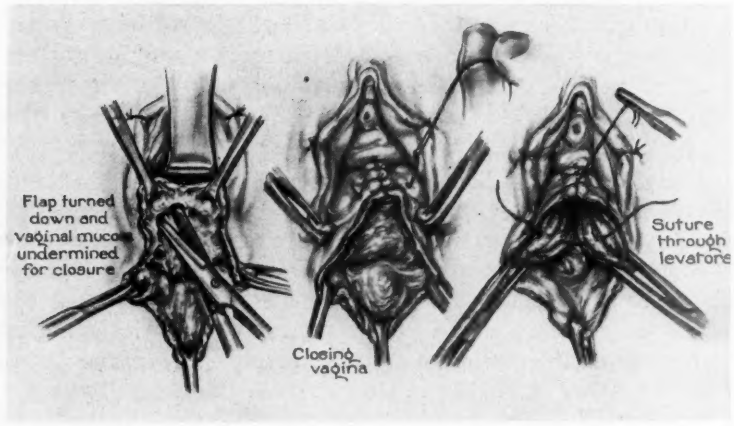

Fig. 2.

proximity to the free margin of the laceration, as illustrated by the dotted line, and is pulled upward by three Allis forceps. A diagram of the relation of the flap to the defect is shown.

Fig. 2 shows the vaginal flap turned down, closing the defect in the anterior rectal wall. The vaginal wall is being undermined by scissors to facilitate the closure. The closure of the vaginal mucosa, the restoration of the urogenital diaphragm, and the obliteration of the dead space is being accomplished by interrupted sutures of No. 1 chromic gut. The levators are being brought together by No. 2 chromic gut.

Fig. 3 illustrates the continued approximation of the levator muscles over the vaginal flap by interrupted sutures of No. 2 chromic gut, and the deep sutures of No. 1 chromic gut approximating the torn ends of the sphincter.

Fig. 4 shows complete closure of the vagina and deep interrupted sutures of No. 1 chromic gut inserted through the constrictor cunei; likewise the levators and the rectal sphincter have been sutured together. Colles' fascia is being closed with interrupted sutures of No. 1 chromic gut. The skin is closed with interrupted

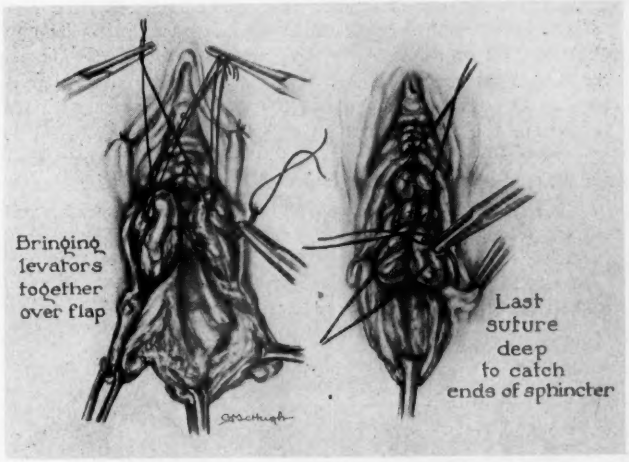

Fig. 3.

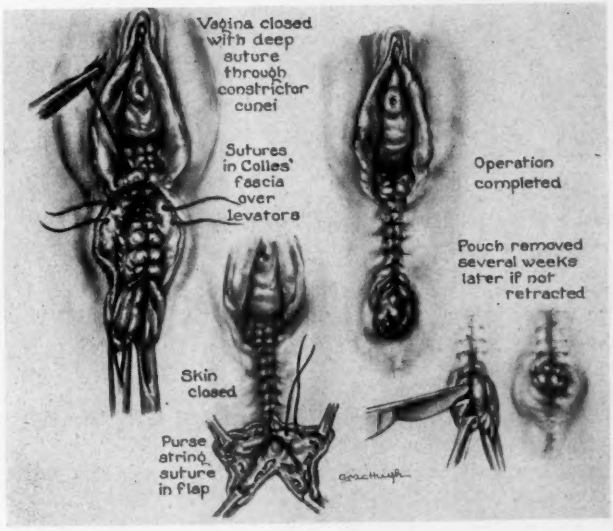

Fig. 4.

sutures of No. 1 chromic gut. The vaginal flap is opened, four Allis forceps are inserted and a purse-string suture is placed in the flap. Finally, the flap is shown after inversion by the purse string. A pouch is being removed several weeks after operation when it fails to retract or shrink down; the final result after removal of the flap is shown.

Fig. 5 is a diagram which shows the relation of the laceration to the anal sphincter and levators, and the relation of the sphincter and levators to each other. The last sketch shows the levators and sphincter drawn together by interrupted sutures.

The postoperative care is equally as important as the preoperative care. The knees are tied together immediately following the operation and kept in that position until the cooperation of the patient is dependable.

One of the opiates, or a combination of lead and opium, is given daily over a ten-day period to keep the patient constipated. On the evening of the ninth day a rectal instillation of warm oil is given and retained. If the patient develops an urge to empty the bowel before the next morning, a low soapsuds enema, small in amount, is immediately given. However, if the patient goes until morning without evacuation, a soapsuds enema is given at that time. In conjunction with the rectal instillations mineral oil or saline cathartics may be administered orally.

During the first few days a retention catheter may be placed in the bladder to prevent soiling of the perineum by urine. A potassium permanganate solution has been used to cleanse the perineum when soiling occurs.

It has been our practice to give no local treatment to the perineum except Zoalite, which has been used in some instances to make the patients more comfortable.

The age of the patients varied from 25 to 64 years, with no small number between 45 and 60 years. The average age was 35 years. The average parity was four. The average duration of the tears in this series was fifteen years. Seventy-six per cent of the tears in the series occurred in primiparas. Eighty-two per cent of the series had forceps operations. Function was restored in the control of the

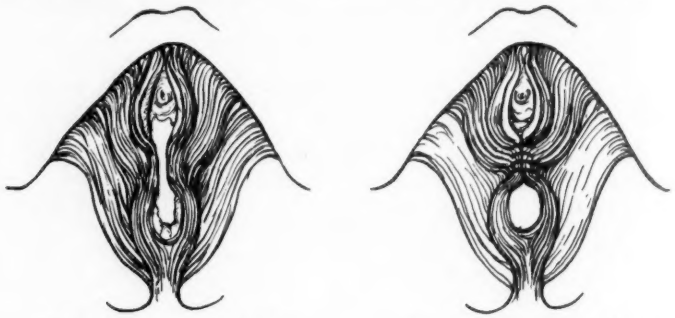

Fig. 5.

fecal stream in 37 of the 39 cases, or 95 per cent. Two cases, or 5 per cent, ended in failure; one developed a rectovaginal fistula with poor control, and the other sloughed the vaginal flap with a complete breakdown of the rectal sphincter. Both of these cases were infected and showed typical temperature elevations; while in the remainder of the series the temperature curves were flat, with the exception of one case which received a good functional result.

It was observed that in only two of the cases had there been a previous attempt at repair. This was a most unexpected finding.

It is interesting to note that in reviewing the records for this series, but not counted in the series, there were five cases of rectovaginal fistulas in which there was incision and conversion comparable to a complete laceration. These cases were repaired by the vaginal flap method and obtained excellent results.

SUMMARY AND COMMENT

1. This series includes 39 cases of chronic complete laceration of the perineum with vaginal wall extension, in which the vaginal flap operation showed a successful result in 95 per cent of the cases. These results compare favorably with those of Miller, Farrar, Phaneuf, and others.

2. Seventy-six per cent of the patients were primiparas.

3. Eighty-two per cent of the patients received a laceration in conjunction with a forceps operation, a most important observation.

4. The average duration of the tear was fifteen years.

5. A previous attempt at repair was noted in only two cases.

6. The technique of the operative procedure taken directly at the time of operation has been reproduced by an artist.

7. All cases were repaired by catgut except five, in which silver wire was used in part. This shows that excellent results can be obtained by catgut alone; and it is my impression that the finer gauge gut is as useful as the heavier. In no instance were continuous sutures used.

8. Infection was a serious factor in only two cases.

9. This operation demands a meticulous and minutely detailed technique.

10. Preoperative and postoperative treatment are essential to a successful end result.

11. The vaginal flap is a protection against postoperative infection and is an excellent procedure for repairing an anterior rectal wall defect.

The illustrations which accompany this article have been prepared by Miss Gladys McHugh.

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DISCUSSION

DR. WILLIAM F. MENGERT, Iowa City, Iowa (by invitation).—In 1882, J. Collins Warren said, "The weak point of every operation hitherto devised, lies in the management of the rectal wound." In order to avoid this, Warren suggested the operation which in slightly modified form has given such excellent results in Dr. Campbell's hands.

Although many different procedures have been employed for the correction of this difficulty, it would seem to be highly desirable to select one which avoids concluding with a fresh rectal wound or a suture line internal to the anal sphincter. Bacteria admittedly are present in the rectum despite the most careful antisepsis, and I believe that no suture line, however made, can completely prevent the penetration of organisms into a newly constructed perineal body during the early postoperative course. The vaginal flap operation as practiced by Dr. Campbell avoids the necessity of leaving a fresh wound within the rectum and places all sutures external to the anal sphincter. The same object can also be achieved by mobilizing the rectum, sliding it downward and re-suturing it to the skin margins of a new perineal body, and external to a reconstructed anal sphincter. The origin of this operation has been credited to Marchand, and the procedure is applicable either to a complete perineal tear involving the vaginal and rectal walls or to high rectovaginal fistulas. In 1902, Noble of Atlanta reported a similar operation, which differed only in the extent of rectal mobilization. Instead of mobilizing the rectum in its entire circumference, only the anterior half is freed and shifted downward. Obviously, this limits the applicability of the procedure to those tears and fistulas which involve not more than the lowermost 3 to 4 cm. of the anterior wall of the rectum.

This operation was recently performed on a young woman with a rectovaginal fistula adjacent but external to the hymenal ring. The anus was dilated and a semicircular incision of the anterior half of the rectum made at the mucocutaneous junction. With a finger in the rectum (Fig. 2) the rectal mucous membrane and muscularis were grasped and carefully dissected until sufficient mobilization without tension had been secured to bring the intact rectum above the fistulous opening to the anal ring. Excess rectum was cut away, and the intact end sutured to the skin of the anus (Fig. 3). Gloves were changed, and the fistulous tract attacked (Fig. 4) and extirpated from the vaginal side.

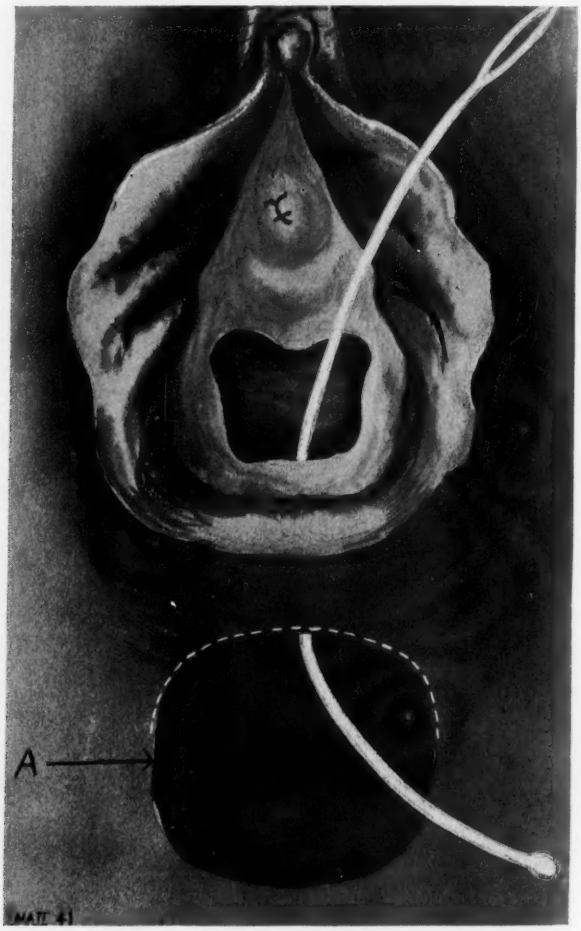

Fig. 1.

When carried out on a patient with a complete tear with extension up the posterior vaginal wall, an incision is made through the edge of the vaginal mucous membrane at its junction with the rectum. The posterior vaginal wall is dissected from the anterior rectal wall with the greatest of care, since a hole inadvertently made into the rectum will jeopardize the entire success of the operation. Once begun, there is generally little scar tissue to complicate or prejudice this dissection, which is carried halfway to the cervix. The remainder of the operation including the repair of the sphincter is similar to the procedure outlined by Dr. Campbell. Using such technique, 8 patients with tears, involving the anal sphincter and 1 to 4 cm. of the posterior vaginal wall, and two patients with rectovaginal fistulas re-

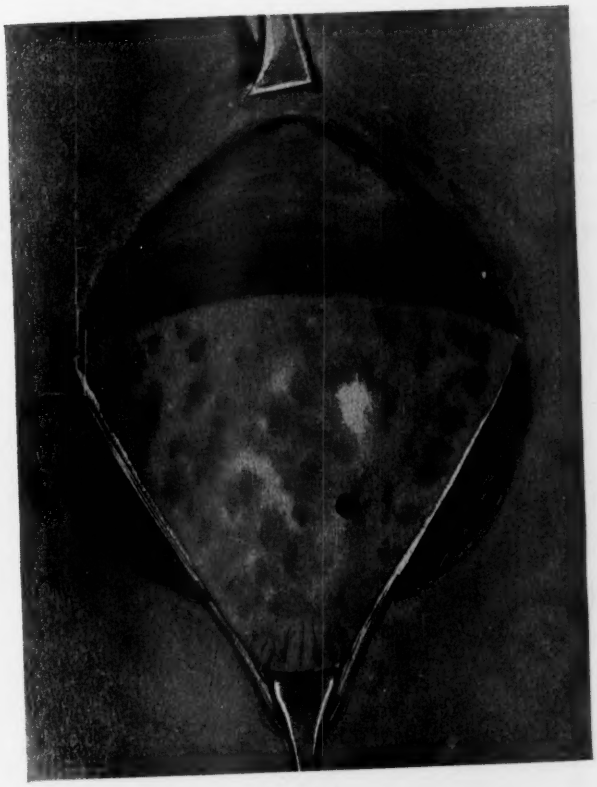

Fig. 2.

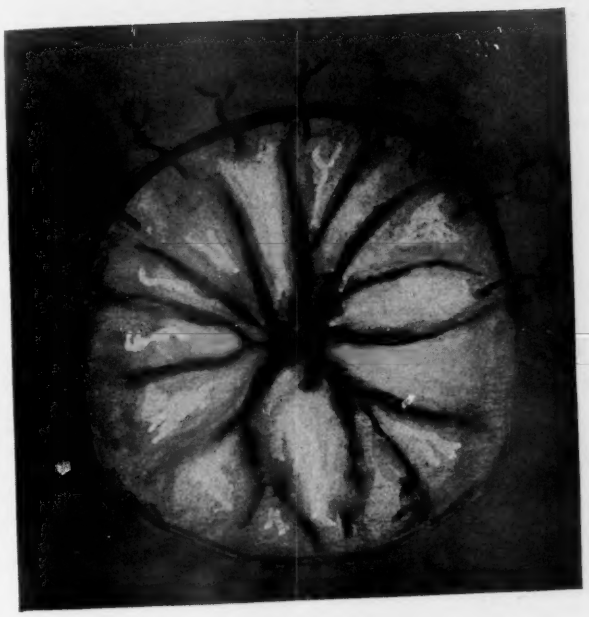

Fig. 3.

ceived an excellent anatomic result and were able to control passage of gas and liquid feces. In another patient with a fistula admitting the index finger, the rectum was mobilized in its entire circumference. Subsequently there was separation of part of the vaginal portion of the wound, but the rectal portion remained intact and control of gas and liquid feces was excellent. There were no failures, and adequate fecal control was secured in each of the 11 patients.

It is felt that the essential principle in the healing of wounds of the rectum and sigmoid is adequate fecal drainage. Since the only wound of the rectum following either the vaginal flap operation or the shifting of the rectal wall is external to the anal sphincter, the danger of inadequate fecal drainage is eliminated.

Fig. 4.

DR. FRED L. ADAIR, CHICAGO, ILL.—It is interesting to note that a considerable percentage of the women reported by Dr. Campbell were in the older age group who acquired these tears thirty-two years ago. While in most of these instances the tears are preventable or repairable at the time of delivery, it would be helpful if we emphasized repair at the time of delivery instead of allowing the patients to go for years without treatment.

So far as the operation itself is concerned, the flap method makes a great appeal to operators where it is possible to acquire a sufficient vaginal flap to bring down and cover the vaginal defect. The defect is sometimes too high to secure a large enough vaginal flap to cover the rectal wall. In those cases one has to restore the rectal mucosa with or without a partial vaginal flap.

We should put the third-degree tears in much the same category that we put vaginal fistulas and recognize that they are the result of neglect at the time of labor. I think our efforts should be directed toward the correction of the traditions that lead to these rather than to operation for repair, necessary as that is.

It is of interest to know that in at least some areas the vesico- and rectovaginal fistulas, and also the third-degree tears, are relatively uncommon. The vesicovaginal fistula formerly constituted a major gynecologic problem. Today it constitutes an individual problem, but in some parts of the country the number is relatively small, indicating very definitely that with improved care both of these extremely troublesome conditions can be minimized if not completely eliminated.

DR. CHANNING W. BARRETT, CHICAGO, ILL.—With these tears we should deal with them when they are a few minutes old instead of after thirty or forty years. The tear that leads to the rectum is almost never so far up but that it can be easily mobilized down to the outlet. This does away with any suture line in the anterior wall, does away with scar tissue that always forms along the line of the tear in the rectum, and avoids having some tissue hanging outside of the rectum.

The injury in complete tear is such that scar tissue forms from one side of the rectum to the other, so that the patient has difficulty in holding liquid feces and difficulty in getting rid of solid feces. If we but turn down a flap which retains that scar in the rectum, the patient still has her stricture. That stricture is one of the things that we should dispose of at the time of operation if it is a complete tear.

In a tear that can be made to stretch up so that it looks some distance up the rectum, or can be made to come down outside the rectum, and if that rectal wall is brought to the outlet with a purse-string suture, then we have the sphincter muscle, not in combination with the levator ani as shown in the picture, but as a little facet on each side of the rectum, and the muscle can be drawn out. That muscle should be picked up on the patient's left side, then a bite of the rectal wall taken well enough up so that the end of the sphincter is well above this edge that we have brought down, and then the sphincter on the other side picked up. When that is tied the two ends of the sphincter should come well above the edge in the median line and then the whole technical work is settled. It is only a question then of putting in the right kind of sutures and getting a good result to make it look as if the patient had had no tear and no recent repair.

In those cases with a fistula, if we use the upper edge of the fistula as the upper edge of the septum and split that, bringing the anterior wall down just as we do in a complete tear not having a fistula, it will make the complete closure just as easy as in a complete tear without a fistula. This method makes the repair of a complete tear almost as sure as the incomplete tear of the rectum. And it is a procedure which can be done immediately if the patient has been delivered under proper aseptic precautions, or, if she has not, there is no use adding to the insecurity and danger of the patient by undertaking to do plastic work in that region. It it better to leave the patient with an open perineum than to close up an infected perineum, and do a perineorrhaphy a little later.

DR. CAMPBELL (closing).—Dr. Adair has brought out in his discussion a most important point, namely the prevention of these tears, but one sees the chronic persistent tears as a result of the poor handiwork of someone else, and should know suitable methods of repair in this complication.

In respect to Dr. Barrett's statement that there is a scar bridging across the perineum which hinders good fecal stream control, the patients that I operated upon were checked and rechecked very carefully, and 95 per cent of them had good control of both solid stool and liquid stool. So that so far as any great amount of scarring is concerned in my cases, I did not see it.

ACIDOSIS AND ALKALOSIS IN OBSTETRICS AND GYNECOLOGY*

W. T. Pride, M.D., James R. Reinberger, M.D., and D. T. Holland, M.D., Memphis, Tenn.

(From the Department of Gynecology and Obstetrics, University of Tennessee College of Medicine)

THE relation of the alkali-acid ratio of the blood to pregnancy is familiar to every obstetrician. Less familiar is the role of the CO_2 combining power of the blood in the complications and occasional fatalities which occur incident to labor and delivery. In the past, shock and death during or after anesthesia for delivery have been attributed to cardiac thrombosis or pulmonary embolism. From current knowledge of the relation of the toxemia of pregnancy to acidosis, it seemed not unlikely that acidosis might also play a part in these unfavorable developments. Accordingly, in the Department of Gynecology and Obstetrics of the University of Tennessee College of Medicine, in 1938, a series of experiments was carried out in an effort to discover a basis for their occurrence in obstetric and gynecologic practice, and methods of their prevention.

Upon a review of these cases, a conspicuous feature was, almost invariably, a long and severe labor. Bearing in mind a possible association of the two conditions, acidosis and long labor, analyses were made of the urine of a number of patients whose labor was prolonged, and in a few cases acetone and diacetic acid were found. Inquiry as to the reason for this finding revealed that, because of the analgesia, and in order to prevent vomiting during anesthesia, patients were given little food or liquid during the course of labor. The acidosis was therefore assumed to be induced by starvation and dehydration. Forced feedings and the intravenous administration of glucose prior to delivery of all patients in labor over thirty hours has served to eliminate this type of acidosis.

Despite the administration of food and liquids, however, patients still suffered from shock following long labors. Estimations of the CO_2 of the blood were therefore made, not only during the first stage of labor, but also during the second stage and immediately following delivery. It was found that the CO_2 combining power of the blood became constantly lower as labor progressed, the lowest point being reached at the end of the second stage. The highest reading of a group of 192 patients in the first stage was 58 volumes per cent, and the lowest 19.6, the average being 42.98 volumes per cent. The majority, therefore, had a moderate acidosis and a number were in a dangerous state, necessitating careful watching. CO_2 estimations during the second stage of labor in 75 cases revealed an average of 40.05 volumes

*Read at the Fifty-Third Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., September 26 to 28, 1940.

per cent, thus showing an intensified acidosis in proportion to the duration and character of labor. The studies made after delivery revealed an average CO_2 of 48.9 volumes per cent, indicating a prompt return to normal. From these findings, it was assumed that the increasing acidosis of the second type was induced by muscular activity and a consequent accumulation of lactice acid in the blood.

To substantiate these observations, it was decided to test the effect of lactic acid upon the CO_2 of the blood. Solutions of 3, 2, and 1 per cent were given intravenously to a number of dogs, with the result that those which received the 3 per cent solution developed hemoglobinuria, respiratory disturbances, and occasionally vomiting, and died. Those given a 2 per cent solution had a mild hemoglobinuria, but recovered, while those given the 1 per cent solution suffered no apparent harm. One gram of lactice acid reduced the CO_2 of the blood 4.3 volumes per cent.

Pursuing this study, another group of dogs was given ether for varying periods, the average being twenty-five minutes, and CO_2 readings were taken at the end of the anesthesia. In none of the animals was the anesthesia carried to the end point; even so, an average decrease of 7.3 volumes per cent in CO_2 was shown. This was in conformity with previous observations that anesthesia produces and intensifies acidosis.

These findings seemed to confirm our theory that the diminished CO_2 combining power of the blood is a significant factor in obstetric complications and fatalities. In order to combat the severe acidosis of prolonged labor, therefore, it was decided to administer sodium bicarbonate to patients who failed to respond to glucose and insulin. Our first experience with this procedure was an unfortunate one. A patient was admitted to the hospital after having been in labor for five days. She was in a state of extreme shock; her blood pressure was low, her pulse rapid, and her skin cold and clammy. No acetone nor diacetic acid was found in the urine, but the CO_2 of the blood was only 15 volumes per cent. Glucose and insulin were administered, without effect. Accordingly, a 2 per cent solution of sterile sodium bicarbonate was given intravenously. The CO_2 of the blood promptly rose and the patient's immediate reaction was favorable. Subsequently, however, she had a relapse and died.

From this experience, it was believed that the combination of glucose and sodium bicarbonate gave rise to a chemical incompatibility which was lethally toxic. This theory was tested by an experiment upon eight dogs. A state of acidosis was first produced in the animals by etherization, and a combination of 10 per cent glucose solution and 5 per cent sodium bicarbonate solution was then given intravenously; all were seized with convulsions and died.

Since sodium bicarbonate had been used successfully in the control of the acidosis of uremia, it was still felt that without glucose or insulin it would have a similar effect upon the acidosis of labor.

Consequently, sodium bicarbonate was given in one-dram doses by mouth to 20 patients during normal labor, the acidosis of dehydration and starvation having first been precluded by food and liquids. In those patients whose labor was not

unduly prolonged nor severe, the CO_2 was increased, an average of 13.2 volumes per cent, whereas the CO_2 was decreased to 4.4 volumes per cent, on the average, in those having long labor. In the latter, the CO_2 could probably have been increased by larger dosage; this, however, was not thought advisable because of the possibility of vomiting. The necessity for the introduction of sodium bicarbonate by some other means was apparent, yet we hesitated to resort to intravenous or rectal injections without some evidence of the reliability of these methods.

Another experiment was then carried out upon 5 dogs, in which alkalosis was produced by the administration of sodium bicarbonate intravenously. Three of the animals received a 5 per cent solution; 2 of these died. One of the 2 died of alkalosis, as manifested by slowing of respiration and hemolysis, while the other had convulsions. The 5 per cent solution had no effect upon the third. A 2 per cent solution was given the 2 remaining dogs without producing any symptoms. The readings revealed that 1 Gm. of sodium bicarbonate elevated the CO_2 of the blood 7 to 8 volumes per cent. Obviously, a 5 per cent solution was dangerous, in that it produced a too rapid and too severe alkalosis, whereas a 2 per cent solution could be administered with safety.

The above experiment was borne out by the intravenous administration of sodium bicarbonate to 2 ante-partum patients, one of whom received 500 c.c. and the other 1000 c.c. of a 2 per cent solution. In the first, the CO_2 of the blood was elevated 15 volumes per cent, and in the second, 15.3 volumes per cent. Neither suffered any untoward reactions. In addition, 3 patients in labor were given sodium bicarbonate rectally; the CO_2 of the blood was not appreciably altered by this method.

In conjunction with these studies, the effect of sedation on the carbon dioxide-combining power of the blood was observed in 20 cases. Moderate doses of sodium amytal apparently had little effect, probably because a moderate dosage of this drug does not produce sufficient analgesia to limit muscular activity.

In 8 of the 20 patients, the CO_2 was increased an average of 13.1 volumes per cent following sodium amytal, whereas in 12 the CO_2 was decreased 11.4 volumes per cent. When hyoscine was added to the sedation, a definite rise in the CO_2 was noted; this was attributed not only to an intensified analgesia and a consequent diminution of muscular activity but also to better pulmonary ventilation. A few patients who had received sodium amytal and hyoscine were given sodium bicarbonate by mouth, with the result that the CO_2 rose from 4 to 24 volumes per cent, indicating the value of sodium bicarbonate as an adjunct to analgesics.

It has been stated previously that a 1 per cent solution of lactic acid administered intravenously corrected alkalosis in dogs without any adverse effect. In order to verify this observation, as well as the findings from experimental intravenous injections of sodium bicarbonate on acidosis, and to further test the harmfulness or efficacy of these measures, it was thought advisable to reverse extreme states of alkalosis and acidosis in dogs.

In three dogs, alkalosis was produced artificially and then reduced with lactic acid. Two of the 3 were given a 3 per cent solution of lactic acid; both developed hematuria but recovered. This strength would be harmful to the normal dog, but in the presence of the extreme acidosis, caused no damage. A 2 per cent solution would, no doubt, have accomplished the desired result without risk. The third dog of the group had a CO_2 reading of 238 volumes per cent at the time of the lactic acid injection, which, of course, is beyond any clinical alkalosis yet reported. Although we were able to reduce the reading to 82 volumes per cent, the animal died.

To another group of dogs in which acidosis had been produced artificially, sodium bicarbonate was given intravenously in 5 per cent solution. Those with a moderate acidosis had little ill effect from the injections, and it was believed that a 2 per cent solution would have been equally successful. One of the dogs died following elevation of the CO_2 of the blood from 7 to 213 volumes per cent.

These studies, apparently, have not only explained the role of prolonged labor and acidosis in shock in obstetric cases, but they have likewise revealed a similar association of alkalosis to many puzzling problems in both obstetrics and surgical gynecology. Although alkalosis is rarely observed in obstetric practice and only occasionally in gynecologic operations, the condition can be no less dangerous than acidosis. Early manifestations are the slowing of respiration, an increase in the CO_2 volume of the blood, hemolysis of the corpuscles, venous congestion, and, in some cases, convulsions.

We have encountered alkalosis in 3 gynecologic patients following rather prolonged gas anesthesia. All 3 were apparently in good condition prior to the operation. Soon afterward, the first patient presented the symptoms of shock, which we assumed was induced by an acute acidosis from the prolonged anesthesia, especially since there was no diminution in urine secretion. She was therefore given normal saline by vein, without effect, and one hour later a blood transfusion, also to no avail. Thereupon, an investigation revealed a CO_2 combining power of the blood of 78 volumes per cent.

The other 2 patients had rather extensive pelvic operations, but were in good condition after the rectal administration of normal saline by the drip method. Several hours later, however, they were reported to be in a state of shock, and when the CO_2 of the blood was estimated, both were found to have a severe alkalosis, rather than an acidosis, as was suspected. Neither patient had vomited, though the pelvic disease was conducive to a lowered vitality.

All three of these patients were observed prior to our experimental work. A 1 per cent solution of lactic acid probably would have corrected the alkalosis had it been recognized before the operation.

In view of the findings from the above experiments, we have felt no hesitancy in administering 1 per cent solution of lactic acid intravenously to patients suffering from alkalosis, or sodium bicarbonate in 2 per cent solution, intravenously, or in hourly dram doses by mouth, to those threatened with the physiologic acidosis of labor. In every case, medication has been regulated according to repeated CO_2 readings. The results have been uniformly gratifying. Since beginning this practice, we have encountered retraction rings in 6 patients; in 2, the rings were promptly relaxed by sodium bicarbonate injections and the deliveries were carried out without further difficulty. We now believe that acidosis and alkalosis can be combated in obstetric and gynecologic procedures if the condition is recognized early, and these measures are carried out under the control of estimations of the CO_2 combining power of the blood at necessary intervals. It should be borne in mind that the combination of sodium bicarbonate and glucose for the correction of acidosis is to be avoided, in that, together they give rise to a chemical incompatibility which is lethally toxic.

DISCUSSION

DR. H. B. VAN WYCK, TORONTO, CANADA.—Some years ago, on Dr. Hendry's service at the Toronto General Hospital, an attempt was made to anticipate dangerous exhaustion by estimation of the CO_2 combining power in any labor prolonged to thirty-six hours. This was not continued, because with the more routine employment of the usual preventive measures, we believed that we were successfully insuring the patient against dangerous exhaustion. In the last twelve months, however, we have had two deaths in the category under discussion.

The acid base disturbance in pregnancy is due to a reduction of total base and not to the accumulation of abnormal acids, and accordingly it has been more correctly termed a compensated alkaline deficit. In eclampsia, however, at the time of convulsions and coma, a true acidosis exists from the accumulation of acids incidental to the muscular work of the convulsion.

Our common clinical experience has shown the value of fluids and glucose in preventing dangerous exhaustion, but Dr. Pride's findings show the ever present potential dangers when the phase approaches an uncompensated CO_2 excess due to lactic acid production, an acid base disturbance where glucose and insulin would naturally be ineffective. The ability of the tissues to handle lactic acid is, however, such that one would expect them to metabolize it between muscular contractions unless the patient suffered from anoxemia. Before the stage of decompensation, even saline tends to safeguard the alkali reserve if the kidneys continue to secrete normally ammonium chloride and acid phosphate.

When the pH of the blood is seriously threatened, however, intravenous sodium bicarbonate therapy would appear logical. One, however, must be on guard against the use of sodium bicarbonate without laboratory control, as an overdose may lead to an alkalosis which is just as dangerous as an uncompensated acidosis. According to Palmer and Van Slyke, to raise the plasma CO_2 one volume per cent requires about 0.026 Gm. of sodium bicarbonate per kilo. In a 60 kilo patient, 1.56 Gm. of sodium bicarbonate would increase the CO_2 by only one volume per cent and 15.6 Gm. only 10 volumes per cent. If one were to give 10 Gm. (500 c.c. of 2 per cent), the effect on the plasma CO_2 would be small and one would think hardly worth while (only about 6 volumes per cent).

At the Toronto General Hospital it has been demonstrated that 500 c.c. of 5 per cent sodium bicarbonate may be given by intravenous drip over a period of two hours without obvious ill effects and with symptomatic improvement. It has been given during the course of administration of glucose to patients in diabetic coma, end-stage nephritis, some cases of leucemia, as well as one case of hyperthyroidism in which postoperative acidosis was severe. Given carefully it appears to be a safe procedure in cases of severe acidosis.

It is also noteworthy that a gradually accumulating acidosis during a long labor is per se a more dangerous phenomenon than the more transitory eclamptic condition, especially if in addition to the other signs of exhaustion supervening, renal deficiency develops.

DR. PRIDE (closing).—Replying to the question, what strength and amount of lactic acid should be given: After much experimenting, we found 1 per cent was safe. This can be given up to 500 c.c. solution, depending upon the patient. Stronger percentages gave trouble. The CO_2 combining power must be checked before giving the solution.

The 1 per cent sodium bicarbonate is entirely safe up to 500 c.c.

The sudden deaths occurring under anesthesia can be reduced to a minimum if this procedure is followed.

HOME DELIVERY SERVICE FOR MEDICAL STUDENTS*

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(From the Baylor University Obstetric Service)

THE preparatory training for home deliveries begins as an introductory course of eleven hours, one hour per week during the third trimester of the sophomore year. This course embraces a general review of the anatomy of the pelvis, pelvic peritoneum, the perineum, the reproductive organs, and the physiology of the endocrines in relation to gestation.

The instruction in the third year consists of a total of eighty-five hours, three one-hour didactic periods per week during the third trimester. During the fourth year, the class is divided into sections, and a total of thirty-two hours is devoted to the study of case records of the deliveries made by the students in the home and the hospital. The student who made the delivery presents this record which includes a complete history, physical and laboratory findings, and history of previous pregnancies and deliveries including this delivery. We encourage the student to admit his errors in his reports, as this is a wholesome mental attitude for both the student and the teacher. The case is then considered by the class and studied as in a pathologic clinical conference.

The teaching in all courses is largely by the question and answer method, discussions, and manikin demonstration, rather than by formal lectures. From this method of teaching, it is gratifying to see members of the class anxious to express their ideas and to pool their information with that of the teacher and their fellow students. Class discussions rather than lectures are more effective and instructive, for facts are fixed in the students' minds by discussion.

In teaching the signs and symptoms of pregnancy to our Junior Class, we try to show why the physiologic changes are present. Why is the diagnosis of pregnancy so difficult to make in the early weeks? Why are there so many modified Friedman and Aschheim-Zondek tests for pregnancy? Is it due to our methods of teaching? Hegar's sign is a positive sign of pregnancy and to recognize this sign requires clinical experience. The place to teach Hegar's sign is in the prenatal clinic where patients in early pregnancy come for diagnosis and instructions. When found to be pregnant, we ask the patient to return frequently in order that students may make bimanual vaginal examinations to familiarize themselves with this physiologic growth and this change in the uterus. We impress the fact that it is necessary for the bladder to be empty to make this examination, a too often neglected procedure.

We know that many errors in a normal delivery are due to the lack of knowledge of the physiologic mechanism of the first stage of labor,

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therefore, we describe, consider, and repeat this important point. Students should know that dilatation of the cervix begins at the internal os and progresses to the external os, and the result of this process is called effacement. As the cervix is effaced, it is retracted slowly but surely over the presenting part, and that sometimes in a primipara, little or no dilatation of the external os may occur until only a very thin portion of the cervix is left. They must know that this process of dilatation, effacement, and retraction, is the physiologic process of labor, and not until the cervix is fully retracted is the first stage of labor complete. A failure to recognize this normal process in some cases may lead to meddlesome obstetrics.

It is in home deliveries that medical students learn the most about normal obstetrics. It is here that they develop confidence in themselves, take measure of their own ability, and visualize for the first time, actual occurrence of presentation, position, and mechanism of labor. I wonder if students would not like to say, "Don't give us a lecture to learn obstetrics, but give us a case in the home to deliver."

We advise our residents, whose position should be recognized, not to be too familiar or patronizing with the students, just a friend and a teacher, for students are cooperative and responsive to suggestions from competent residents, and from the teaching faculty. Caution should be exercised in selecting residents who have the ability, personality, and character, and who are interested in teaching clean and efficient obstetrics whether it be in the home or in the hospital. We like our residents to have that uncommon gift of common sense.

The students take full charge of the deliveries but are responsible to and under the supervision of the resident. Any abnormal findings must at once be reported to the resident, and if the residents are not available, then to one of the dispensary obstetricians on service at the time. All major pathologic cases who visit the antenatal clinic, or develop complications before or at the time of delivery, are admitted to the hospital for further care, study, and delivery. Only non-complicated cases are delivered in the home.

A complete record on each case must be submitted by the student to the resident within ten days after the service is completed. These records are marked "poor," "good," or "excellent," by the resident, received by the Dean, and are considered in the student's final grades.

Home Delivery Service is limited to senior students who serve in pairs, and who have the privilege of selecting their own partners. The pairs of students serve in sequence for a period of seven days, on each service through the following assignments: (a) Prenatal Clinic, (b) Parkland (city, county) Hospital, (c) Home Delivery Service (second call), (d) Home Delivery Service (first call).

The prenatal clinic is held daily from 10:00 to 12:00 A.M. in the hospitals. Cases are assigned to the students for history, physical examinations, laboratory tests, and when completed, the charts are presented to the instructor for discussion and for a check of the students' findings.

During the Parkland Hospital Service, the students live in the hospital, do their clinical clerkship, observe the progress of labor, and assist in the deliveries under the direct supervision of the members on the obstetric staff.

In order to receive the obstetric calls for the students, a twenty-four-hour telephone service for home deliveries is maintained through Baylor University Hospital. Patients are cared for in all parts of the city, including two smaller adjoining municipalities and at times outside the city limits within reasonable distance. Students furnish their own automobile transportation, but obstetric bags completely equipped are supplied through the university outpatient department. Before entering upon the home delivery service, the resident gives individual instructions to the students concerning preparation and draping of the bed and patient before delivery.

Under the supervision of the resident, the students are responsible for all phases of the delivery in the home, from the first steps in the preparation and draping of the patient on through the actual delivery, postpartum care, and care of the infant. We do not have the finances to employ nurses for this service, but we believe it is of benefit to the student to assume the duties of a nurse in order that he may better know his responsibilities and learn to appreciate clean obstetrics. It is our purpose to make the home delivery service so thorough, practical, and efficient, that the student will on graduation know that the delivery of a baby is a physiologic process, and rarely is operative interference necessary. If necessary, it should have been recognized during the antenatal period.

When students receive calls, they promptly go to see their patient and make the following observations and preparations:

1. Take a history—inquire as to the frequency and duration of uterine contractions.
2. Determine position and presentation by abdominal and by rectal examinations, and estimate the amount of effacement and dilatation.
3. If time is sufficient, an enema is given.
4. After a physical and obstetric examination, a first preparation is done by shaving and washing the perineum with tincture of green soap.
5. An abdominal buckle binder is applied.

The student remains in the home with the patient and observes the frequency, intensity, and duration of uterine contractions, and records his findings. During the course of ensuing labor, careful check of her progress is made by rectal examinations at frequent intervals, and the student reports his findings to the resident.

The preparation for delivery of a primipara is made when the head begins to crown, and usually in a multipara when effacement and dilatation of the cervix is 8 to 10 cm. This information is ascertained by rectal examinations made by the student, and one marvels at the aptness of the student to grasp this situation. Our preparation in the home is about the same routine as we use in the hospital. The field of operation is again cleaned with soap and water, sponged with alcohol, and one-half strength tincture of iodine is applied. The patient is then draped. During this preparation, one student scrubs his hands while the other takes the

part of a utility nurse. The medical student who is serving as a nurse, places an ironing board under the mattress for support and prepares the table for sterile drapings and supplies. The student who is making the delivery has scrubbed his hands, dried them, and has put on his sterile gown and gloves. Draping of the patient is as follows: The assisting student lifts the patient up, and a large sterile sheet is placed over the bed and under the patient's buttocks. The legs are still held so that sterile boots, which are long enough to extend to the vulva, can be slipped on the patient's legs. A sterile sheet is placed over the abdomen, with towels placed over the abdominal spread and over the top of each boot. The towels on the boots are held by rings. During the delivery, a towel is used to protect the anus. Immediately after the patient is draped, the bladder is emptied. If the patient is in the second stage of labor, she is told to bear down during the uterine contraction, at which time the assisting student gives the patient chloroform. In the delivery of the head and during a contraction, a moderate pressure is made on the vertex of the baby to prevent a too rapid extension and expulsion which we believe is a more effective way to prevent injuries to the baby and lacerations of the perineum. Chloroform is used, and is given at the beginning and for the duration of the uterine contractions, and then removed and not given after the delivery of the head. Slow delivery and gentleness in delivering the head and shoulders of the baby are advised, and at no time is traction put upon the head. The baby is dried with a towel, the mucus aspirated from the throat, and when this is completed, 1 per cent silver nitrate solution is placed in the baby's eyes. Under ordinary conditions, the cord is not ligated until pulsation stops, as we sometimes think the baby may receive a little more blood from the placenta, and more time is given for the separation of the placenta. The baby is laid aside in a warm blanket and later cared for by the assisting student.

Attempt at delivery of the placenta is not made until the fundus of the uterus has ascended above the umbilicus, and then during contraction, gentle pressure by Credé method is made. Upon delivery of the placenta, the membranes are best detached by pushing the uterus further up into the abdomen while gentle traction is made on the placenta. We do not use the various methods of twisting or pulling on the placenta, because we feel that this may account for retention of membrane and elevation of temperature in the puerperium. The field of operation is cleaned, and peri-pads with T-binders are applied. After forty-eight hours, all dressings are removed and pads placed beneath the buttocks for drainage. No other dressings are applied. Soap and water are used externally for cleanliness.

The patient is advised to change position frequently and to make herself comfortable. A general diet is permitted and mineral oil is used after the second day. Instructions concerning lactation are given, and she is taught that the mammary glands are organs of secretion and not reservoirs. We do not credit a rise of temperature to engorgement of the mammary glands, but should elevation of temperature occur, it is probably due to puerperal infection. Daily post-partum calls are made by students for the first five days, then every other day until the tenth day, then as indicated.

STATISTICAL RESULTS

From July 1, 1937, to March 1, 1939, 4,000 consecutive deliveries in the Obstetrical Service in Baylor University Hospital, Florence Nightingale division, were made: 44.4 per cent, or about 1,700, were patients delivered by private physicians, 55.6 per cent, or about 2,300 were on the charity service, 436 of which were delivered in the hospital. A rise of temperature to 100.4° F., or above, for two or more consecutive days occurred in 94 charity cases in the home and hospital. It was found that temperature elevations occurred most frequently in those patients who had prolonged labor, with some type of operative obstetric procedure necessary for the termination of labor.

There were four maternal deaths on the charity service and none in the private service. The causes of the deaths were two cerebral hemorrhages following labor

in hypertensive cases, one fulminating toxemia, and one puerperal infection. In the 4,000 cases we had 59 cesarean sections, 5 in the charity, and 54 in the private cases.

Of 1,364 cases on our charity service from July 1, 1939, to June 30, 1940, 212 were delivered in the hospital and 1,152 in the home. Those delivered in the hospital showed one puerperal infection; one maternal death occurred in a patient who had paresis and died suddenly during labor. Those delivered in the home showed 4 puerperal infections. There were three cesarean sections out of 1,364 cases.

CONCLUSION

A home delivery service for the student does not retard initiative and resourcefulness, but stimulates independent growth. This course teaches that one should not become too dependent on the hospital amid comforts, but that the hospital is the fort for cases of complication. We teach that pregnancy and labor are normal processes, and by being clean and conservative, it can still be done safely in the home.

DISCUSSION

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—The steadily increasing hospitalization of women for labor might make it appear as if the instruction of medical students in home deliveries is no longer necessary in this present day and age. Estimates have been made which show that during the last twenty years institutional births have mounted in some of our large cities to as much as 80 per cent of the total number of deliveries. It might prove an ideal situation if the advantages of a hospital delivery could be accorded to all pregnant women.

One may be inclined to doubt, however, this claim that universal hospitalization would be completely ideal; for we find that the triad of fatalities included in hemorrhage, toxemia, and sepsis claims perhaps as many victims in the hospitals as in the homes. And to what may this be ascribed? There is widespread, although perhaps somewhat mistaken, belief that a hospital spells safety but this, in a sense, is far from the truth. It is the character of the hospital which is the deciding factor, for not all hospitals so-called are necessarily good hospitals. Moreover in the country at large there are not enough institutional beds available to provide ideal conditions for all our pregnant women. The supposed advantages of a hospital confinement also carry in their train an increased incidence of operative deliveries, interferences with the normal processes of labor, indiscriminate employment of methods of pain relief, and the loss of that important virtue of the obstetrician, namely the exercise of patience. I would not decry for one moment the convenience of hospital deliveries, both for the patient and the physician, but to claim that the institution is the sole recourse is to indulge in an exaggeration.

The foregoing remarks may seem a divergence from Dr. Hannah's presentation. However, I make them as an endorsement of his thesis that a home delivery service is an essential factor in the training of our medical students, in order to cultivate their self-reliance and their practical application of theoretic teaching. In no other way can the gap between theory and practice be bridged so successfully. The observation of a delivery in a well-equipped hospital operating room is very desirable, but it fails to engender in the student that respect for the patient and her environment, that close contact through the waiting hours, that necessary reliance on his personal ability and perhaps conscience. All of these are essential to his success as an obstetrician. He is taking care of Mrs. Jones in the tenement house and not a case from Ward B.

Dr. Hannah has done a good service in calling renewed attention to the value and success of an out-door obstetric teaching service. He stresses the adequate preparation and close supervision of the students. He points to the desirability of an association between the out-door service and a hospital, and the record of morbidity and mortality in his institution is an enviable one. One may differ

perhaps with certain details in his procedures, such as the conduct of the third stage and the use of chloroform as an analgesic. But these are matters of opinion. The maintenance of asepsis is admirable, but one may wonder whether the local application of alcohol and half strength tincture of iodine is tolerated by a wide awake patient without objection. I would also like to ask how many deliveries are made as an average for each student, for numbers count when practical experience is to be evaluated.

Notwithstanding the drift to hospitals, many women for years to come necessarily will be confined in their homes by their family physicians. It is well for the physicians to know how it may be done with safety for their patients and with credit to themselves. I feel that the example set by Dr. Hannah and by others who are engaged in this work, deserves our commendation and not the reproach which is sometimes meted out to them in certain quarters that shall be left nameless. It would be of interest and value to have a country-wide study made of the general scope and the results obtained in these student obstetric services. Perhaps this Association may be prevailed upon to undertake the task.

DR. GRANDISON D. ROYSTON, ST. LOUIS, MO.—Ample hospital facilities are usually available in urban areas. Eighty-five per cent of the births in St. Louis during the past year occurred in hospitals.

In the Washington University Clinic we attempt to deliver in the hospital *all* primiparas and those multiparas with any complication. Six or seven years ago, we had about 425 home deliveries per year, but for the past three or four years the number has ranged from 163 to 181 per year. Smaller communities and rural districts have a larger proportion of home deliveries. In some of these, the small poorly equipped hospital may be less desirable than the home for the delivery of normal cases.

Are medical schools preparing their students to care safely for these home deliveries? The present tendency to minimize their necessity would seem to invite or encourage in the students a careless indifferent attitude toward their importance.

Dr. E. T. Bruning, of Santa Ana, California, emphasizes that the present lethargic attitude of the medical profession toward the importance of home deliveries has been due to lack of proper equipment. Schwarz and Bruning developed a 35-pound portable delivery table, known as the Washington University delivery table. We have employed this table satisfactorily in the Washington University home delivery service for the past three years. Bruning has also developed a set of paper drapes that can be sterilized for one hour in the autoclave under 20 pounds' pressure. These are not opened until the patient is ready to be draped, and are burned immediately after use. This minimum handling lessens the dangers of infection that may be communicated through the laundry or attendants, in case of washable cloth drapes. Washable cloth drapes are often too few or too thin to offer reliable protection after they are once wet, while the paper drapes are less permeable and have had no contact with other drapes.

This discussion is not to be construed as advocating a preference for home over hospital deliveries. It is a plea for preparation of medical students in obstetrics, so that they can do safe work wherever they may be called, and many of them can profit by being taught ordinary surgical cleanliness and adaptability in home deliveries.

DR. IRVING W. POTTER, BUFFALO, N. Y.—I agree with Dr. Hannah in what he has said on what the average doctor seems to know about the beginning of labor. The men with whom we see cases are divided into two classes. The first class are those doctors whose patients are usually not in labor when we are called. We generally go at once to the second group of men because they need help, and usually have waited too long with the more complicated cases. There are plenty of men doing obstetrics who attempt to deliver a woman who is not in labor. It is very important to recognize the effacement of the lower uterine segment and important to know when it is complete, also when the os is dilatable. An opening that you can put your finger in with no effacement does not mean an immediate delivery.

DR. JAMES L. REYCRAFT, CLEVELAND, OHIO.—We have a very large service in Cleveland under our direct supervision. The out-patient deliveries at the Maternity Hospital are done by the students and amount to about 2,000 a year. We have 1,500 a year on the in-service at the Cleveland City Hospital, and in addition about 100 cases a month on the in-service at the Maternity Hospital.

I want to emphasize the matter of supervision. If you can have an organization that gives adequate supervision, it makes for better obstetric habits. A student is going to learn more about obstetrics in the long run if he is very closely supervised. We allow them to see deliveries in the hospital, and when they go on a case in a home they are permitted to make a vaginal examination to determine the progress of the case and whether the measurements are adequate. The patients in whom difficulty is expected are sent to the hospital. If the student finds the case is a normal one, usually a multipara, he makes an examination and reports in. When the patient has progressed normally and is near to delivery, the assistant resident goes out. He is directly responsible to the resident, who in turn is responsible to one of our visiting obstetricians. A delivery nurse is usually present. We require twelve deliveries by these men and they usually get from twenty to twenty-five deliveries on their out-patient service.

DR. WARD F. SEELEY, DETROIT, MICH.—It is true that a large percentage of deliveries, at least in the rural districts, do occur in the home. The same is true for most cases of measles, fractures, pneumonia, etc., but no other department of medicine feels that it is necessary to go into the home and teach their students at the bedside. I think our attitude is a hold-over from the time when we did not have hospital facilities sufficient to teach medical students and therefore had to carry our teaching into the homes of the patients.

I agree that a student is probably a better obstetrician after having had the experience of a home delivery service, but I also believe that he first should have had his experience in the hospital and that adquate supervision should be provided in order that he does not make the same mistake time after time without correction. I believe that this supervision should be provided for by sending him out with an instructor rather than with a resident.

I disagree with Dr. Hannah on the matter of equipment. I think the student should be sent out with a minimum of equipment. We do not attempt to carry the hospital to the patient but rather to teach our students to work aseptically with material and under conditions as they will find them in actual practice.

DR. HANNAH (closing).—Dr. Kosmak has asked a question about the giving of chloroform by our students in home deliveries. We believe that chloroform in labor, if carefully given and the patient not too rapidly and deeply anesthetized, is comparatively safe. We are fully aware of the danger of the use of chloroform, and the students are so taught. Had we the financial means we would probably use nitrous oxide gas.

We do not have nurses to accompany the students on home deliveries. Nurses are an excellent asset for this work, but we have learned the educational value to the medical student who assumes the duties of a utility nurse. What better way have we to teach than by actual doing? The student who makes the delivery scrubs and prepares himself as the obstetrician who makes a delivery in the hospital, while his co-worker acts as a utility nurse and anesthetist. Our students are taught to report every hour, or every two hours, to the resident, and more often if in doubt as to the progress of labor. Our residents are expected to go to the student's aid, and if they find complications or are in doubt as to the prognosis, the patient is brought promptly to the hospital. In home deliveries, if the occasion arises, we permit our residents to apply low forceps when the head is arrested on the perineum, do episiotomy and repair. Forceps in this sort of case is usually applied without any anesthetic and traction is made only during uterine contraction, at which time a few drops of chloroform may be given.

We teach that the student, resident, and the staff doctors should not take anything for granted. We, as others, would enjoy the comforts of hospital facilities,

but we believe home delivery is a better way to teach clinical obstetrics. We deliver approximately 100 patients per month in Parkland Hospital, probably 25 patients in Baylor Hospital, and 80 to 110 patients in the homes. This is a fair estimation of our charity work in the Obstetrical Department of Baylor University College of Medicine. Each of our students will deliver from 35 to 50 patients before graduation and quite a number of them may deliver more. It is interesting to see how proud the student is when he returns from a successful delivery, even though he has spent hours on the case. It is the responsibility; it is the anxiety; it is the moral support given to the student by his resident and staff members during a home delivery that teaches him that pregnancy and labor can still be conducted safely in the home.

Obstetric departments of medical schools are fully aware of the difficulties of teaching obstetrics as compared with the teaching of medicine and surgery. In these branches the clinical material is hospitalized and complete preparation of the patient is made for the clinician and a definite time is arranged for the students and the teachers, while in obstetrics the irregular hours and the indefinite time of delivery cannot be arranged. Medical students should be required to make home deliveries that they may better learn that the development of a mental attitude towards the practice of medicine is acquired through responsibilities and the experience of anxious hours.

NATIONALITY AND CARCINOMA OF THE CERVIX*

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REALIZING that poverty and multiple parturition are constant factors in carcinoma of the cervix, I[1] (in 1928 to 1930) attempted to find additional factors by personally interviewing 226 patients suffering with cervical carcinoma, and by comparing this group with a comparable number of noncancerous patients selected as controls because of their age, multiparity, and similar economic status. Several possible additional factors were found. The comparison of the two series as to nationality (reproduced as Table I) was passed over rather briefly as having little significance.

TABLE I. COMPARISON OF THE TWO SERIES AS TO NATIONALITY

NATIONALITY	CARCINOMA		CONTROL	
	NO.	%	NO.	%
Black	20	8.8	31	15.3
White	206	91.1	171	84.6
German	20	8.8	17	8.4
Italian	74	32.7	30	14.8
Jewish	15	6.6	33	16.3
Greek	2	0.8	0	0.0
Irish	45	19.4	52	25.7
Polish	8	3.5	3	1.4
Others	42	18.5	36	17.8
Total cases	226		202	

Horwitz[2] had previously reported that at the Mayo Clinic the disease was only one-fourth as frequent in Jewesses as in Gentile women. While

*Read at the Fifty-Third Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., September 26 to 28, 1940.

cancer of the cervix was known to be prevalent among Italians, their relatively large proportion in the cancer series was dismissed on the assumption that Memorial Hospital had a large Italian clientele.

TABLE II. COMPARISON OF NATIONALITY IN SELECTED GROUPS CLASSIFIED AS TO DIAGNOSIS

NATIONALITY	CARCINOMA OF CERVIX		CARCINOMA OF CORPUS		CARCINOMA OF OVARY		CARCINOMA OF VULVA		BENIGN	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Total	226		445		221		115		2,273	
Black	20	8.8	14	3.1	4	1.8	5	4.3	178	7.8
White	206	91.1								
German	20	8.8	35	7.6	12	5.4	7	6.0	187	8.1
Italian	74	32.7	32	7.1	9	4.0	10	8.6	198	8.6
Jewish	15	6.6	85	19.6	47	21.2	9	7.8	812	35.5
Greek	2	0.8	0	0.0	0	0.0	0	0.0	33	1.4
Irish	45	19.4	83	18.6	7	3.1	18	15.6	363	15.8
Polish	8	3.5	2	0.4	0	0.0	1	0.8	69	3.0
English	0	0.0	0	0.0	11	4.9	0	0.0	198	8.6
Austrian	0	0.0	12	2.6	16	7.2	5	4.3	82	3.5
Others	42	18.5	25	5.6	12	5.4	2	1.7	25	1.0
Not recorded	0				13	5.7				
U. S. A.	0	0.0	157	35.2	90	40.7	58	50.4	128	5.6

In an attempt to compare the nationality incidence in cervical cancer in this series with that of patients suffering from other gynecologic lesions, consecutive records as filed have been studied, but the numbers used in each classification are not the entire number of patients filed under that diagnosis; i.e., this is a cross section of the clinic in the years studied rather than the total number of cases in the clinic. The high Italian and low Jewish incidence in cancer of the cervix as compared with that of the other gynecologic lesions is the outstanding feature of this study. Since the carcinoma of the cervix series only included patients who gave the opportunity for personal interviews, the number was necessarily small. For this reason it seemed advisable to study all the records of patients having primary carcinoma of the cervix, and who were treated at Memorial Hospital from 1916 to 1937. The 3,106 patients studied are classified as to nationality in Table III.

TABLE III. TOTAL CERVIX CASES CLASSIFIED AS TO NATIONALITY

NATIONALITY	NO.	%
Black	225	7.2
German	341	10.9
Italian	528	16.9
Jewish	132	4.2
French	54	1.7
Irish	419	13.4
Polish	32	1.0
English and Scotch	330	10.6
Austrian and Hungarian	104	3.3
Dutch, Spanish, Belgian, Japanese, Swiss, unclassed	91	2.9
Greek	10	0.3
U. S. A.	764	24.5
Danish, Swedish, Finnish, and Norwegian	76	2.1
Total	3,106	100.0

The Italian, Irish, and Scotch-English groups appear in this order of frequency, with Jewesses having an even smaller incidence than in the smaller group. Having found in the continuation of this study an Irish-Catholic married to a man named Cohen and classified as a Jewess, this presentation was held up from 1937 to the present date in order personally to question the living patients suffering from cancer of the cervix as to their race and nativity. The error of race and nationality as filed was found to be less than 0.1 per cent and, therefore, negligible.

TABLE IV. COMPARISON OF PERCENTAGES OF NATIONALITY INCIDENCE IN THE SEVERAL TYPES OF GYNECOLOGIC LESIONS

	CERVIX	CORPUS	OVARY	VULVA	BENIGN	CLINIC	
	%	%	%	%	%	NO.	%
Black	7.2	3.1	1.8	4.3	7.8	426	6.9
German	10.9	7.6	5.4	6.0	8.1	582	9.4
Italian	16.9	7.1	4.0	8.6	8.6	777	12.5
Jewish	4.2	19.6	21.6	7.8	35.5	1085	17.5
Greek	0.3	0.0	0.0	9.0	1.4	43	0.06
Irish	13.4	18.6	3.1	15.6	15.8	890	14.4
Polish	1.0	0.4	0.0	0.8	3.0	104	1.6
English and Scotch	10.6	0.0	4.9	0.0	8.6	439	7.1
Austrian	3.3	2.6	7.2	4.3	3.2	219	3.5
U. S. A.	24.5	35.2	40.7	50.4	5.6	1191	19.3
Others	6.7	5.6	5.4	1.7	1.0	412	6.6
Total	3106	445	221	115	2281	6168	

Comparison of the total primary cervical carcinoma incidence with the other individual lesions and with the total cross section of the clinic shows the Italian and Scotch-English groups to be considerably higher in the cervix group than in the other groups. The Irish incidence is about the same in all groups. The Jewish incidence in the cervix group is strikingly low by comparison with the other individual lesions and with the clinic cross section. The German incidence is slightly higher in the cervical group. Since the cervix cases are more than half of the total cases studied and this being a perhaps undue influence on the total clinic cross section figures, these two classifications have been compared with the total noncervical lesions used, and the results are shown in Table IV A.

TABLE IV A. COMPARISON OF NATIONALITY INCIDENCE IN PATIENTS WITH CERVICAL AND NONCERVICAL LESIONS AND WITH A CROSS SECTION OF THE ENTIRE CLINIC

	CERVIX		CLINIC		NONCERVICAL	
	NO.	%	NO.	%	NO.	%
Black	225	7.2	426	6.9	201	65
German	341	10.9	582	9.4	241	7.8
Italian	528	16.9	777	12.5	249	8.1
Jewish	132	4.2	1085	17.5	953	31.1
Greek	10	0.3	43	0.06	33	1.0
Irish	419	13.4	890	14.4	471	15.3
Polish	32	1.0	104	1.6	72	2.3
Scotch and English	330	10.6	439	7.1	109	3.5
Austrian	104	3.3	219	3.5	115	3.7
U. S. A.	764	24.5	1191	19.3	427	13.9
Others	221	7.1	412	6.6	191	6.2
Totals	3106		6168		3062	

Here again the relatively high Italian and Scotch-English incidence, the constant Irish incidence, and the low Jewish incidence in carcinoma of the cervix is shown by the comparison.

TABLE IV B. COMPARISON BY PERCENTAGES OF NATIONALITY INCIDENCE IN THE SEVERAL TYPES OF GYNECOLOGIC LESION WITH THE TOTAL PERCENTAGES AVERAGE

	CERVIX	CORPUS A	OVARY B	VULVA C	BENIGN D	TOTAL AVERAGE	AVERAGE A B C D
Black	7.2	3.1	1.8	4.3	7.8	4.8	4.2
German	10.9	7.6	5.4	6.0	8.1	7.6	6.7
Italian	16.9	7.1	4.0	8.6	8.6	9.0	7.0
Jewish	4.2	19.6	21.6	7.8	35.5	17.7	21.1
Greek	0.3	0.0	0.0	0.0	1.4	0.8	0.3
Irish	13.4	18.6	3.1	15.6	15.8	13.3	13.2
Polish	1.0	0.4	0.0	0.8	3.0	1.3	1.0
Scotch and English	10.6	0.0	4.9	0.0	8.6	7.3	3.3
Austrian	3.3	2.6	7.2	4.3	3.2	4.1	4.3
U. S. A.	24.5	35.2	40.7	50.4	5.6	31.2	32.8
Others	6.7	5.6	5.4	1.7	1.0	4.0	3.4

This is a comparison of each individual lesion nationality incidence expressed in percentages and in total average percentages and total average noncervical lesion percentages. This substantiates the results of Table IV and IV A, except that when considered by percentage averages, negroes show a higher incidence of cervix cancer than of other gynecologic lesions.

TABLE V. COMPARISON BY FIVE-YEAR GROUPS OF NATIONALITY INCIDENCE

	1915-20		1921-25		1926-30		1931-35		1936-37	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Black	12	3.0	47	6.1	61	7.2	69	8.9	36	10.8
German	42	10.7	76	9.8	101	12.0	86	11.1	36	10.8
Italian	61	15.5	128	16.6	145	17.2	123	15.9	71	21.3
Jewish	17	4.3	23	2.9	28	3.3	46	5.9	18	5.4
French	7	1.7	10	1.3	13	1.5	8	1.0	6	1.8
Irish	65	16.5	108	14.0	102	12.1	109	14.1	35	10.5
English and Scotch	48	12.2	83	10.8	90	10.7	81	10.5	27	8.1
U. S. A.	107	27.2	226	29.4	214	25.4	151	19.5	67	20.1
All others	34	8.6	67	8.6	87	10.3	98	12.7	37	11.1
Total (3,106)	393		768		841		771		333	

It has been suggested that the incidence of carcinoma of the cervix in Jewesses is increasing. Various reasons are offered for this suggestion. These will be taken up later in the discussion of these statistics. Table V compares the incidence of various nationalities during five-year periods. Only the nationalities having the more prominent incidences are included so that the total in the table does not equal that shown in previous tables. It is notable that the incidence in Jewesses does not increase. Blacks do show some progressive increase in their incidence at Memorial Hospital and Italians do show some increase in the period 1936-1937, but no previous progressive incidence.

Probably twenty-year periods would present better evidence of increased incidence with succeeding generations. However, the available records do not permit statistical study previous to 1916.

TABLE VI. COMPARISON OF NATIONALITY INCIDENCE (EXPRESSED IN PERCENTAGES) OF FIVE-YEAR PERIODS AND TOTALS IN CARCINOMA OF THE CERVIX

NATIONALITY	1915-20	1921-25	1926-30	1931-35	1936-37	TOTAL 1915-37	
						NO.	%
Black	3.0	6.1	7.2	8.9	10.8	225	7.2
German	10.7	9.8	12.0	11.1	10.8	341	10.9
Italian	15.5	16.6	17.0	15.9	21.3	528	16.9
Jewish	4.3	2.9	3.3	5.9	5.4	132	4.2
French	1.7	1.3	1.5	1.0	1.8	54	1.7
Irish	16.5	14.0	12.1	14.1	10.8	419	13.4
English and Scotch	12.2	10.8	10.7	10.5	8.1	330	10.6
U. S. A.	27.2	29.4	25.4	19.5	20.1	764	24.5
All others	8.6	8.7	10.3	12.7	11.1	313	10.0

Similarly Table VI compares the nationality by percentages with the total figures of those nationalities included in the table.

TABLE VII. COMPARISON AS TO NATIONALITY OF LIVING, DEAD, AND TOTAL PATIENTS WITH CARCINOMA OF CERVIX

	BLACK		ITALIAN		IRISH		JEWISH		U. S. A.		TOTALS
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	
Living	46	6.8	135	20.2	83	12.9	50	7.4	124	18.5	667
Dead											
1915-25	56	5.2	166	15.4	160	14.8	35	3.2	313	29.1	1,074
1926-37	123	9.0	227	16.6	176	12.8	47	3.4	327	23.9	1,365
Total											
1915-37	225	7.2	528	16.9	419	13.4	132	4.2	764	24.5	3,106

Table VII was compiled to study the significance of nationality as to prognosis. Italian and Jewish patients seemed to show an increase in percentages of living over dead patients for each of the 1915 to 1925 and 1926 to 1937 periods, and over the total dead of the corresponding nationality. Since the length of life with the disease is not stated, this does not prove that the prognosis is any better for the Jews and Italians than for any other nationality.

DISCUSSION

There must be some reason for the relatively low Jewish and high Italian incidence in carcinoma of the cervix. Several theoretical suggestions are of interest but no adequate explanation has been found. These suggestions are discussed as follows:

Sexual Activity and Multiparity.—Bagg[3] has shown that "repeated forced breeding" in rodents tends to increase the incidence of breast and genital cancer. Knowing multiparity to be a constant factor in cancer of the cervix, it has never been shown that Jewesses were far behind Italian or Irish women in either fertility or multiparity. Questions on sexual activity asked of patients with carcinoma of the cervix failed to obtain cooperative or accurate answers.

Poverty.—Cancer of the cervix is found almost exclusively in the ward or clinic type of patient, rarely being seen in the type of patient who can afford private care. This suggests poor obstetric and post-partum care and neglect of symptoms of the lacerated and ulcerated cervix. One gets the impression in New York City that Jewesses are more liable to consult the clinics for symptoms of cervicitis than are the Italian or Irish women.

Circumcision.—Naturally the well-known rarity of cancer of the penis in circumcised men has led to the suggestion that this is in some way a factor in the

low incidence of cervix cancer in Jewesses. It was my impression that in the obstetric hospitals in New York City most male babies are circumcised before leaving the hospital, regardless of race or religion. Inquiry revealed that this is true of private patients but that less than 30 per cent of the male babies in the wards are circumcised before leaving. This included Jewish babies. It remains for someone to show whether the retained foreskin with its associated smegma bacilli is, or is not, a factor in cervical carcinoma.

Bacteriologic.—In an attempt to find a virulence index of vaginal organisms preoperatively, Ruge,[4] Philips,[5] and Clareberg[6] studied the vaginal flora of normal women and of women with cancer of the cervix. In the cancer patients various types of streptococci increased and predominated with staphylococci to a lesser degree. However, they made no attempt to classify their patients according to race. I know of no comparative studies on the vaginal flora of noncancerous Jewesses and Italians, nor of patients with cancer of the cervix, as to racial differences in vaginal flora.

Hygiene.—A study of the laws of hygiene of Jewish people[7] reveals the information that for seven days after menstruation a Jewess is considered unclean and is forbidden sexual intercourse. A cleansing bath and douche are advised before resuming sexual relations, but undoubtedly this is not peculiar to Jewesses. By questioning patients in the clinic at Memorial Hospital no marked difference has been detected in the chemical type of douches used by Jewesses and Italians. The suggestion that perhaps Jews as well as Gentiles of the present generation were not as orthodox in their religious behavior as their ancestors is not substantiated by any increase in cervical cancer incidence, as the result of any lapse of orthodox behavior.

Diet.—No marked difference has been detected between Italian and Jewish diets except in shell fish and the forbidden meats. Practically all other meats in New York City come from cattle slaughtered by the Kosher methods; meat for Jews differing only in that it is slaughtered by a special agent having the necessary religious qualifications. It is doubtful if this could play any part in the difference in cancer incidence.

Inbreeding.—Experimental laboratories are well aware that certain strains of rodents are "tumor resistant" while other strains are "tumor susceptible." Some strains are resistant to some types of tumors and susceptible to other types. These qualities can be maintained by inbreeding, thus maintaining a pure strain. Cross breeding lessens the resistance. The well-known reluctance of Jews to marry out of their own race may have some significance in their maintaining a low incidence of cancer of the cervix. Certainly Jewesses are not resistant to other types of genital and breast cancer.

CONCLUSIONS

1. In carcinoma of the cervix the relatively low Jewish incidence and high Italian and Scotch-English incidence is established in contrast with the nationality incidence of the remainder of the Gynecological Clinic at Memorial Hospital.

2. Various theories for this incidence have been discussed but no adequate explanation has been found.

3. The most plausible explanations deal with circumcision and other racial customs.

4. Further studies on the racial differences in vaginal flora are suggested.

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DISCUSSION

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—Statistics, such as Dr. Smith has presented, must be interpreted very cautiously. At the County Hospital in Chicago, the percentage of Italians having carcinoma of the cervix is small and bears a direct relationship to the number of Italians admitted to the hospital. The highest incidence of carcinoma of the cervix occurs in the negroes, Poles, and Germans. These races also have the greatest number of admissions to the hospital. If statistics from different hospitals vary in this manner, other factors than nationality must play a role.

Practically all statistical analysis of this sort do, however, indicate that Jewesses, although they have no racial immunity to cancer, are less susceptible to cancer of the cervix. The factors which contribute to this lower incidence are not clearly understood. It has been suggested that the practice of circumcision among Jews is a factor, on the basis that the infected glans penis in the uncircumcised male may carry to the cervix the infection which by chronic irritation results in carcinoma.

Handley quotes an interesting observation concerning Fiji Islanders. In these Islands, there are 90,000 natives and 70,000 immigrated Indians. These races do not intermingle. The Fiji Islanders practice circumcision at puberty. The Indians do not. Hospital records in Snowa for a period of eight years, from 1925 to 1932, show only three cases of cancer of the cervix in Fijian women and 26 cases among Indian women. A similar study applied to our own population might throw some light on this subject.

Another factor, which it has been suggested may contribute to the lower incidence of cancer of the cervix among Jewish women, is the practice of Mosaic law, namely the cleansing after the forbidden period. This argument also is based on the premise that chronic infection and irritation are the forerunner of cancer of the cervix. Schiller, however, states that carcinoma of the cervix arises, grows, and develops before any signs of infection, erosion, or chronic irritation are demonstrable. In his opinion, chronic irritation is seldom a contributing factor to cancer of the cervix.

In this connection, some observations we made in 1932 on the influence of radium upon the bacterial flora of the female genitalia may be of interest. For some weeks or months following adequate x-ray treatment, bacteria disappeared completely from the vaginal discharge. After three to six months, there is a reappearance of the cervical and the vaginal flora. This reappearance of the cervical and the vaginal flora is often the forerunner of a recurrence of the malignant tumor. This does not necessarily indicate, of course, that the infection is a factor in the recurrence. However, I do think that Dr. Smith's suggestion that the vaginal flora in different races should be studied is a very pertinent one.

A SKIN TEST FOR THE DIAGNOSIS OF PREGNANCY*

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THE use of skin reactions as an aid in clinical diagnosis of many conditions has long been recognized as a valuable procedure. The Von Pirquet, Schick, Dick reactions and the use of various proteins intradermally for the purpose of detecting allergic sensitivity have all proved their clinical usefulness. There are so many biologic differences between pregnant and nonpregnant individuals that the possibility of being able to differentiate between these groups by means of a skin reaction to some antigen seemed not too remote.

Falls and Bartlett,[1] in 1914, attempted to extract a protein from the placenta which might be used for this purpose. The results were unsatisfactory, due to the fact that the methods employed were not sufficiently refined to yield a pure protein as was hoped, but a mixture of proteins was obtained which led to nonspecific reactions. By using better methods of extraction and preparation of the placental proteins, Cohen and Freda[2] attempted to produce precipitin reactions and specific skin reactions that might be useful diagnostically. When the precipitin reaction was tried, serum of known pregnant women reacted positively in about 75 per cent of the cases. The serum of males and normal females did not react. Certain nonpregnant women with gynecologic pathology gave a rather high percentage of false positive reactions which nullified the usefulness of this method for practical diagnostic purposes.

The use of placental tissue extracts in producing skin reactions was to some extent successful, since about 75 per cent of the patients tested by intradermal injections gave positive reactions if pregnancy existed and negative if no pregnancy were present. This result was in accord with the results reported by Esch,[3] Englehorn and Wintz,[4] Gruskin[5] and Schwartz[6] who made similar tests have reported a higher percentage of correct diagnosis.

The high percentage of false reactions (25 per cent) rendered the use of these procedures for diagnostic purposes useless, and so it was decided to try to find an antigen that would give more specific reactions.

The possibility of using proteins extracted from breast tissue was suggested, since it was thought that during pregnancy the cells of the breast might secrete a protein of somewhat different composition than other body proteins. On further consideration this idea was rejected in favor of using colostrum which must contain the proteins produced by the breast in early pregnancy. By using this material the contamination of

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the pure breast proteins by blood and other tissue proteins was avoided. These we felt might produce nonspecific reactions as in the case of the placental extracts.

Accordingly, it was decided to use colostrum in various dilutions intradermally on pregnant and nonpregnant women to determine if they reacted alike or differently under these conditions. We were rather surprised to find that pregnant women gave a faint response or no reaction to the injections and nonpregnant individuals reacted rather vigorously. These results seemed to be quite constant. As the number of patients injected increased, the high percentage of correct diagnosis made by the test became quite significant.

PREPARATION OF MATERIAL

Colostrum from primiparous pregnant women is expressed from the breast manually into a sterile glass container after cleansing the nipple and areola with ether. It was found that the colostrum was most easily obtained at about the twenty-eighth week of pregnancy. It was then diluted with equal amounts of sterile normal saline solution. To 10 c.c. of this mixture 1/10 c.c. of 1 to 100 merthiolate solution was added as a preservative, and it was kept in the icebox.

TECHNIQUE OF INJECTION

The flexor surface of the forearm of the patient is sponged lightly with a piece of cotton saturated with ether. A weal is formed by injecting exactly 1/50 of a c.c. of the diluted colostrum intradermally, using a tuberculin syringe and a 26 gauge needle for the purpose. A second syringe and needle are used to make a similar-sized weal with physiologic salt solution a few inches lower on the arm. This is to be observed as a control. The reaction is noted at ten minutes, one-half hour, and one hour. Readings made at the half hour are usually sufficiently marked to indicate whether the test is positive or negative.

If the patient is pregnant, the weal produced by the injection of colostrum will appear pearly, resembling a fresh mosquito bite with little or no pinkish areola surrounding it. The site of injection will scarcely be recognizable in an hour, except for the needle prick in the center. The control produces no reaction beyond the raised area caused by the injection.

When the patient is not pregnant, a marked difference in the reaction is seen. The weal tends to remain raised and pearly until a few minutes after injection when it begins to increase in diameter, eventually becoming two to three times the size originally produced by the injection, without changing in color. There then appears an areola of pink to red one to two inches in diameter which is irregular in contour, color, and depth and projects lymphangitic pseudopodiums from its periphery. The reaction steadily grows in intensity for an hour and persists for four or five hours. The control injection with physiologic salt solution in these patients gives neither increase in the weal or areola pigmentation.

RESULTS

Our report deals with the injection of 265 known pregnant women in various stages of pregnancy and includes toxic as well as nontoxic cases.

The controls comprise 358 known nonpregnant cases of which 100 were adult males, 45 were children below the age of fifteen, 50 menstruating women, 50 postpartum cases, and 113 cases of either normal nonpregnant women or women with various known gynecologic conditions, carcinoma, fibroids, ovarian cysts, etc. Finally 50 unknown problem cases were tested to establish the diagnosis.

Of the 265 pregnant women described as known to be pregnant, in approximately 50 cases the test was applied before the fourth month, although the signs and

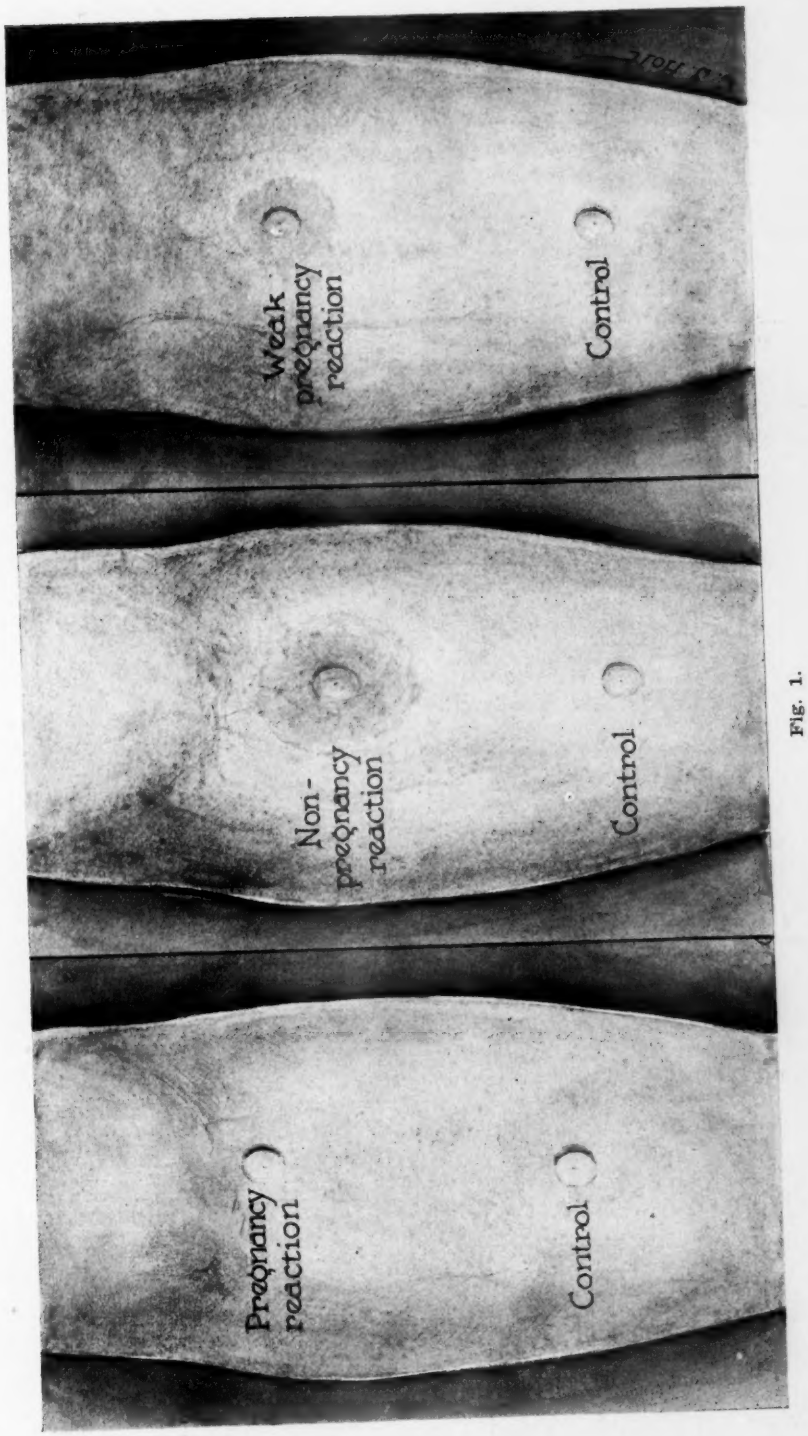
Pregnancy reaction
Control
Non-pregnancy reaction
Control
Weak pregnancy reaction
Control

Fig. 1.

symptoms were sufficiently marked to lead us to make a clinical diagnosis of probable pregnancy later confirmed. The rest of the 265 women had sufficiently advanced in pregnancy to give positive signs of pregnancy. In this group there were 5 false reactions. In 2 women nonpregnancy reactions were obtained and the patients later were shown to have a living fetus in the uterus. One of these later gave a positive pregnancy reaction, and the other failed to return for retest.

There were 3 cases in which a weak reaction indicated nonpregnancy. However, this reaction persisted for only forty-five minutes and had disappeared by the end of the hour contrary to the reaction seen in nonpregnancy. Early in pregnancy and toward the end of pregnancy a slight reddening around the vesicle produced by the injection might be termed a weak or false nonpregnancy reaction. It differs from the true nonpregnancy reaction in the width of the areola, the depth of color, and the fact the weal does not enlarge after injection. It differs from pregnancy reaction in that there is some color around the weal. A similar reaction has been seen in the early puerperium. A group of 15 patients were tested during labor, and it was seen that the stage of labor made no appreciable difference in the reaction which was similar to the weak nonpregnancy reaction just described.

One hundred and thirteen known nonpregnant females were tested. Forty-five of these were out-patient gynecologic cases and 68 were patients in the gynecologic wards, mostly postoperative cases at Cook County Hospital. Typical nonpregnancy reactions were obtained in all but 4 cases in which a typical pregnancy reaction was obtained, which would have led to an incorrect diagnosis if the test alone had been relied upon.

On further study of these false reactions, the 4 women who gave this reaction were all in the menopause, not having menstruated for from five to seventeen years. Three of these cases were advanced Group III carcinomas of the cervix uteri, and the fourth was a simple procidentia seventeen years after the last menstrual period.

Fifty menstruating women were studied; all of these gave nonpregnancy reactions. Five cases were studied throughout the menstrual period.

A group of 45 children of both sexes were studied, varying in age from 2 to 15 years. A reaction similar to that seen in pregnancy was obtained in all cases up to the age of about 10 years, at which time modified nonpregnant reactions were seen in both males and females.

One hundred male patients of varying ages from the medical service of the Cook County Hospital were studied. These were routine medical service patients with cardiac disease, hypertension, blood dyscrasia, etc., as is customarily found in a medical ward. None of these gave positive pregnancy reactions. Three of them gave modified nonpregnancy reactions; one was a boy of 15 and the others were elderly men, 65 and 75 years of age.

There were 50 post-partum cases varying from two to eight weeks postdelivery. In all but 3 of these the reaction was that of nonpregnancy. This was noted whether or not the patient was nursing her baby. The 3 pregnancy reactions were all in women eight weeks post partum, one was menstruating, the other two admitted exposure, but sufficient time had not elapsed to determine whether or not pregnancy existed. In the puerperium therefore it would seem that the test was correct in 96 per cent of the cases. Obviously the test would rarely be applied in such cases for the practical purpose of diagnosis.

DISCUSSION

The interpretation of the reaction is not so simple. From a consideration of the foregoing results, it appears that nonpregnant individuals have become sensitized to a specific protein contained in colostrum from primiparous women. This protein probably is not contained in human milk or in colostrum or milk obtained from the cow, since injections made using these substances as controls gave no specific reactions comparable to those obtained with human colostrum. If it is present, the specific reaction is masked by other substances in these biologic materials. Human milk taken as soon as the breasts began to secrete milk (three to four days after delivery) and used

for injection failed to give a specific reaction. The colostrum of multiparous women frequently gave a slight nonspecific reaction in both pregnant and nonpregnant individuals. Attempts to extract the active principle of colostrum obtained from primiparas, which is responsible for these reactions, using oil, ether, alcohol, ammonium sulphate for extraction, or dializing through parchment membrane, resulted in failure. It would seem that dilution by milk, alteration of the breast function by previous pregnancy, and attempts at purification by chemical methods, all alter the substance responsible for the test in a manner which prevents the characteristic response on injection.

Various dilutions of colostrum were tried and different amounts were used. When undiluted colostrum was injected the reaction was more marked, and some of the pregnant women showed a weal and areola approaching that seen in nonpregnant women. When more than one-fiftieth of a cubic centimeter was used similar side reactions were obtained. This is in line with the experience of the men working in the field of allergy (T. Nelson[7]).

To determine whether a nonspecific protein other than milk proteins would give these reactions, gelatin was used as a control in some cases. No reactions were obtained in the amounts used. Further work is in progress in an attempt to obtain the active substance in pure form.

The failure of the pregnant woman to react to the injection we feel is best explained by the assumption that early in pregnancy the production and absorption of the active substance from the breast leads to an immune state which prevents the local reaction at the site of injection, except the weak reaction seen in about 80 per cent of the cases in the first six and the last three weeks of pregnancy, during labor, and in the early days of the puerperium. The weak reactions seen at this time are difficult to explain. It is possible that toward the end of pregnancy the breast may cease producing the specific substance responsible for the reaction. The weak reactions begin to appear about two weeks from term and the typical nonpregnant reaction begins to appear about the twelfth to fourteenth day of the puerperium. Naturally the test will not be applied clinically at the end of pregnancy or during the puerperium so that the weak reactions seen at these times are of only academic interest.

As a matter of interest 5 menstruating women were injected daily throughout their periods, to determine what effect if any this would have on the reaction. These patients react as nonpregnant women the first day of the period, and the reaction gradually decreases on the following days. They react as pregnant women on the last day. The reaction gradually returns to the nonpregnant type after three or four days. This is significant because of the false conclusions that might be drawn from tests performed at this time of the month. It is not clear what influences this change unless the breast stimulation produced by the menstrual cycle at this point leads to absorption from the breast of sufficient amounts of colostrum to produce a temporary immune reaction.

The negative reactions seen in children before puberty would suggest that they have not yet produced and absorbed enough of this protein to become sensitized to the colostrum injections.

The reaction of the males to injected colostrum suggests that the male breast secretes sufficient of the specific solution over a period of years to sensitize but not immunize the patient. On the whole the reactions obtained in males have been of less intensity than those seen in nonpregnant females. This may be due in part to differences in the skin texture.

Older patients, both male and female, gave a reaction of diminished intensity which decreased progressively with the increase of age. This may be explained by the assumption that breast activity gradually decreases, finally ending sensitization. We realize that the explanation of these results is far from complete at this time and further work is in progress to attempt to prove or disprove some of our ideas.

Two patients with ectopic pregnancy, one with an unruptured isthmic pregnancy (six weeks) and one with an aborting ampullary pregnancy (ten weeks), gave pregnancy reactions, the correctness of which were confirmed by operation.

The most interesting group were the problem patients in whom the test was applied to try to make the diagnosis of early pregnancy one to three weeks after missing the first period. The difficulty here is the fact that very early pregnancies theoretically may be present, produce a reaction, terminate by death and expulsion of the fetus without producing sufficient clinical evidence to prove or disprove the presence of pregnancy. In a few cases we have been able to hospitalize the patient and make sure of the diagnosis, in others we have had to depend on clinical observation which we realize is open to some objection. In spite of this, we have been able to make the correct diagnosis in 46 cases in which sufficient time has elapsed to prove or disprove the correctness of the diagnosis as measured by the test.

It is important to note that considerable familiarity with the test is necessary for the correct interpretation of the reactions produced. After doing about 25 tests in pregnant and nonpregnant individuals, the interpretation of these reactions is quite simple. This is in accordance with the experience of others who use intradermal injections of antigens for diagnostic purposes. From our present experience, we are sanguine regarding the diagnostic value of the test. If our results are confirmed by others, it will make the diagnosis of early pregnancy much simpler, quicker, and more economical than the methods we now have at our command.

CONCLUSIONS

1. An intradermal injection of a colostrum solution gave no reaction in 98 per cent of pregnant women.
2. Nonpregnant women reacted to similar injections with the formation of a characteristic weal and areola in 96 per cent of cases.
3. Males reacted similarly to nonpregnant females.
4. Children before puberty reacted similarly to pregnant women.
5. The test seems to have value as an aid in the clinical diagnosis of pregnancy.

We wish to acknowledge the assistance and cooperation of Professor William H. Welker of the Department of Physiological Chemistry in the preparation of the antigens and his part as consultant in the pursuit of this research.

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DISCUSSION

DR. LAWRENCE M. RANDALL, ROCHESTER, MINN.—We now have two accepted tests for pregnancy with an accuracy proved to be more than 98 per cent from long experience, the Friedman and the Aschheim-Zondek. One must compare any new test to this standard regardless of the time factor involved in the two tests mentioned.

A large number of so-called tests for pregnancy have appeared in the past twelve years; their average incidence of error may very reasonably be put at 20 per cent. Perhaps a smaller incidence of error will occur in the hands of one who is expert in the taking of histories and their interpretation and who is expert in physical examination. One who is less expert in such matters and who relies upon a relatively inaccurate laboratory test may actually increase his percentage of errors.

A certain number of errors will always occur with any "pregnancy test." These tests are for the detection of substances present in bodily fluids or secretions that are most commonly associated with the presence of pregnancy but which may be found in association with other conditions.

Skin tests, based on the intradermal injections of protein substances, depend upon allergic reactions and are therefore subject to the errors common to such tests. Allergic individuals who are sensitive to many foreign proteins may give a reaction that is false as far as pregnancy is concerned. The ovaries of the nonpregnant rabbit and the immature mouse are much more specifically sensitive than is the skin. One must be familiar with wheal formation to minimize the personal error of interpretation. An error of 10 per cent is probably to be expected from this source, with the placental extract used in the method of Gruskin.

However, much as one may distrust skin tests as a whole, we cannot help but be impressed with the results that Dr. Falls and his co-workers have obtained with a simple and logical experiment. They have presented a very thorough piece of work and conservatively asked for further trial by themselves and others.

DR. A. J. RONGY, NEW YORK, N. Y.—The test described by Dr. Falls is an important addition to the already established pregnancy tests. It may help to solve the diagnosis in early unruptured ectopic pregnancy. Last week, one of my associates was confronted with the difficulty of diagnosing an unruptured ectopic pregnancy in a young woman. The ordinary Aschheim-Zondek test on a rabbit and a mouse proved to be negative. The pathologist then made a definite diagnosis of pregnancy upon sectioning the ovary of the mouse, basing it on microscopic changes in the cells of the ovary. The patient was operated upon and was found to have an early unruptured tubal pregnancy.

DR. FALLS (closing).—I appreciate the fact that when considering skin reactions there is no test which gives 100 per cent of correct readings. The Wassermann test has its limitations, as do the Widal and all of the allergy tests. Yet in spite of these limitations these tests have stood the test of time and are useful clinically. We hope that our test will also stand the test of time which will determine its value.

One must do a number of these tests to become familiar with the reaction before beginning to depend upon them to make a clinical diagnosis. We feel that the interpretation after about 25 tests should familiarize one with the reaction sufficiently to make his judgment correct.

The paper reports the diagnosis of two unruptured ectopic pregnancies proved by operation. The other day we had a case in which we suspected an ectopic preg-

nancy. We operated and found an old hematosalpinx. The fetus had been dead for some time. The reaction was negative for pregnancy in spite of the fact that the hematoma in the tube probably had been produced by an ectopic pregnancy.

If this test does prove its merit, it is obvious how valuable a test that can be read in an hour and at the expense of a little salt solution and colostrum will be as an addition to our diagnostic armamentarium.

OBJECTIONS TO INDUCTION OF LABOR IN NORMAL PREGNANT WOMEN*

EDWARD L. CORNELL, M.D., F.A.C.S., CHICAGO, ILL.

THIS discussion is limited to the induction of labor in the normal pregnant woman, the woman who has no toxemia, no disproportion, no disease. In the past ten years advice to induce labor on the mildest indications is increasing rapidly in the literature. Convenience of the patient, wishes of the patient or her family, convenience of the physician, living a distance from the hospital, desire to have the delivery occur in "working hours," have all been brought forward as indications for the induction of labor. I doubt not but that many of our noted obstetricians long since dead, must be clamoring to rise again and take issue with this type of "streamlined" obstetrics.

May I call your attention to the dangers, physical and legal, which are always present when one interferes with the normal processes of pregnancy and labor.

Many authors state that the size of the baby indicates whether or not the patient is at term or over-term. From my own experience and from observation, I know that experienced physicians miss the weight of babies before birth as much as two pounds. In the series of patients included here, there are two who went over-term as we usually compute the term from the menstrual period. One patient was thirty-three days over and her baby weighed 3,295 Gm. The other was thirty-two days past term and the baby weighed 4,250 Gm. This is quite a difference in weight.

The x-ray film can give an idea of the size of the baby, but even with that aid, experienced physicians many times miss the weight by pounds. A well-known obstetrician of my acquaintance insisted upon a cesarean section upon a patient who he said had a very large baby. The baby weighed under 6 pounds. Polyhydramnios caused the large uterus.

Some couples whose eugenic history is such, naturally have large babies. This is seen frequently in patients who deliver ahead of schedule. Two patients in this series delivered 4,400 Gm. babies one week before expected term and another ten days after the expected term. The largest baby, which weighed 4,515 Gm., was delivered twenty-three days past the expected term. On the other hand, I have seen babies who weigh from 5 to 6 pounds present all the signs of prematurity. Koff and

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I am indebted to Dr. Paul W. Sweet for securing the statistics for this paper.

Potter say, "unfortunately there is no reliable sign or collection of signs by which antenatal diagnosis of abnormal size of the fetus can be definitely established except perhaps in extreme cases." To this I agree. In my opinion, therefore, we cannot safely predict that a patient is at term, or past term, by the size of the baby.

Most of us put considerable reliance on the date of the last menstrual period in predicting the time of delivery. We know that periods may be very irregular. We are beginning to realize that ovulation is also irregular as to time. Such being the case, it is conceivable that a patient could have had a delayed ovulation or period at the time she became pregnant. Again there are those who menstruate only four to six times a year. I recall years ago having a patient who delivered a baby weighing less than 6 pounds exactly one year after her last period. Surely we could not classify that pregnancy as postmature. If we accept the term of pregnancy as 273 days and ovulation as necessary before pregnancy, then a patient who ovulates just previous to a period should arrive at term later than a woman who ovulates in the middle area of the intermenstrual period.

The date of the period, therefore, is not an accurate guide.

We have tried to gauge term from the date of quickening. Several years ago I made a detailed study of this point on 750 cases from private practice. The women were intelligent and cooperative. They were as accurate as one could expect. The menstrual and life dates were known. A student of higher mathematics was given the job of working out a formula, and when we were all through, no accurate formula could be deduced. The error was as great for the life date as for the menstrual date.

The life date, therefore, cannot be used as an accurate guide.

What are the common complications of induction which are not usually seen in spontaneous labor? The outstanding one is prolapse of the cord. Practically without exception all writers mention it. The report of the Central Association of Obstetricians and Gynecologists shows that prolapse of the cord is three times more frequent in 1,669 induced cases. Plass reports a rate of nearly 1 per cent.

With few exceptions the fetal mortality seems to be higher in induced cases. In my personal experience this is true, because early in my practice I induced labor more frequently. It is much more difficult to explain the death of a baby to the distressed parents when labor has been induced. One should not forget that it is better to have a live baby past term than a dead one at or before term.

Placental infection is reported to be much greater in induced labor. Penfold and Butter report 61 per cent of the placentas of induced cases were infected, against 24 per cent in spontaneous cases of labor. They state that the longer the postinduction period the greater the possibility of placental infection. Mixed infection of the placenta holds greater danger for the child than single infection. In 15 of the 46 cases of induced labor with infected placentas, the child died. In seven stillbirth cases only two had no infection in the placentas or fetus. In five deaths

after birth, the organism found in the child was also present in the infant. The maternal morbidity was nearly 50 per cent in the 46 cases reported.

While it is true that many writers report that their morbidity rates are not higher in induced cases, I know by experience that interference in any manner which involves vaginal manipulations raises my morbidity rate in spite of anything I may do about the technique in the delivery rooms. I am sure the same bacteria are lurking around delivery rooms all over the country. Perhaps the thermometers vary so the readings are not so high or the patient's temperature is taken less frequently. Whatever it is that is different, I cannot bring my morbidity rates down to the same level as the rates among the patients who deliver spontaneously.

Post-partum hemorrhage is increased in induction cases and is mentioned in many articles in the literature. While it is true that hemorrhage is more frequent in pathologic cases, it cannot be overlooked as a source of trouble in normal women.

The use of oxytoxic drugs always carries a very definite hazard. I need not stress to this Society the fact that rupture of the uterus, extensive lacerations of the cervix, and brain hemorrhage are common sequelae. The use of quinine in large doses is said to have a bad effect on the ears of the fetus. I have seen 3 to 5 gr. doses of quinine produce terrific contractions of the uterus. One multipara in my practice delivered in thirty minutes following a 5 gr. dose of quinine. Her cries of pain could be heard throughout the hospital.

From the legal standpoint, I believe we are courting trouble if some patient should be inclined to take issue with us after delivery, especially if the baby should be injured or die. W. C. Woodward is quoted by DeLee as follows:

> No professional standard anywhere at any time could justify a physician in doing anything that would jeopardize the life and well-being of mother or infant solely for the physician's convenience. Moreover, consent by the father or mother, even with a thorough understanding of the matter, would not excuse a physician who deliberately expedites labor solely for his own convenience, to the material danger of mother and child.
>
> It may be questioned whether a physician can lawfully do anything to expedite the onset of labor unless it is necessary to do so for the life of mother and baby—A child might have a right of action against the physician who is responsible for the injury—notwithstanding anything the parents may have authorized to be done in conduct of labor.

There have been many indications for induction of labor in normal pregnant women. Slemons, in 1932, gave nervousness in woman past term, previous precipitate labor, and living a distance from the hospital as indications in some 35 to 50 cases. Other authors have mentioned convenience of the patient and the doctor, solicitation by relatives, and many other flimsy reasons. We might as well say that we should do cesarean sections on all these patients, using the same indications.

My observations of patients delivered by obstetricians in my own city who induce labor is that in many cases the cervix and the vagina are badly torn and scarred. The history in most of these normal patients is

that of a tedious attempt to put the patient into labor by means of medicine, bag, rupture of the membranes, bougies, or a combination of two or more. In many the cervix did not dilate and Dührssen's incisions were made. In others pituitrin or thymophysin was used and the cervix torn as a result of the strong uterine contractions.

Many authors mention certain conditions which should be present before an attempt is made to induce labor. F. J. Iiams lists them as follows: (1) Patient under observation for months, (2) patient's health perfect, (3) past history good, (4) no disproportion or malposition, (5) pregnancy advanced to eight and one-half months, (6) baby must weigh 6 pounds or more, (7) cervix must be soft, effaced or partially dilated.

It is easy to determine the first four conditions, but the last three are open to marked variations in interpretation. Iiams mentions that his smallest babies weighed 5 pounds 2.5 ounces and 5.5 pounds. How many more weighed less than 6 pounds is not recorded.

For the purpose of this article a series of 200 consecutive normal pregnant women were studied. Data were secured similar to that used by other authors in an effort to influence the medical profession to interfere with pregnancy at or near term. All patients who presented signs of toxemia or any of the accidents of labor were eliminated. What do we find?

1. The average age of all was 28.6 at delivery.
2. There were 91 primiparas and 109 multiparas.
3. The average weight of all babies was 3,507 Gm. The largest weighed 4,515 Gm. and the smallest 1,814 Gm.

TABLE I. WEIGHT OF BABIES

DAYS BEFORE OR AFTER TERM	LESS THAN 2,500 GM.	2,501-3,000 GM.	3,001-3,500 GM.	3,501-4,000 GM.	4,001-4,300 GM.	4,301-4,515 GM.
−7 to 0	3	8	28	20	4	2
1 to 7	2	9*	35	22	6	
8 to 15		3	15	17	5	1
16+			6	8	5	2
Total	5	20	84	67	20	5

*One set twins.

TABLE II

DAYS + OR − TERM	AVERAGE AGE	PARITY I	II	III	IV+	AVERAGE WEIGHT, BABY, GM.	NO. BABIES WEIGHING 4,000+ GM.	AVERAGE LENGTH LABOR 1ST STAGE HR.	2ND STAGE HR.	3RD STAGE HR.	NO. FORCEPS DELIVERIES	WEIGHT OF LARGEST BABY, GM.	WEIGHT OF SMALLEST BABY, GM.
−7 to 0	28.4	30	24	6	5	3,347.4	6	11.15	42+	7.9	26	4,400	1,814
1 to 7+	28.8	32	22	13	6	3,356.8	6	9.57	41.5	7.4	38	4,200	2,325
8 to 15+	28.6	21	11	8	1	3,565.5	6	12.52	44.8	6.8	20	4,400	2,675
16+	28.7	8	6	3	4	3,765.5	7	9.41	43.5	6.8	12	4,515	3,060
Grand average or total	28.6	91	63	30	16	3,507	25	10.54	42.9	7.2	96	4,378	2,468

4. Twenty-five babies weighed 4,000 Gm. or more, about equally divided in the following groups:

5. The delivery dates being known and the expected term dates being computed, the 200 patients were divided into four groups: (A) Those who delivered in the interim between seven days before term and the expected term; (B) those who delivered one to seven days past the expected term; (C) those who delivered 8.15 days after expected term; (D) those who delivered sixteen days or more after expected term.

TABLE III

AGE	PARA	WEIGHT GM.	LABOR			NO. DAYS +	REMARKS
			1ST STAGE	2ND STAGE	3RD STAGE		
32	iv	3,510	1:45	7	7	16	
35	ii	3,295	15:30	83	7	33	Forceps
28	ii	3,444	5:35	9	5	20	Forceps
31	ii	3,770	7:15	15	5	16	
25	i	3,487	20	207	11	26	Forceps
41	iii	4,360	10:50	15	4	17	
25	i	3,665	12:25	57	6	17	
20	i	3,595	21:30	48	16	28	Forceps
28	i	3,670	Too rapid			16	Forceps
22	i	4,155	19:25	77	4	25	Forceps
32	iv	3,146	1:15	24	8	22	
28	ii	4,085	2	46	9	20	
24	i	4,515	27:10	1:10	6	23	Forceps
26	iii	3,900	2:30	25	8	18	
40	ii	4,165	12	44	6	18	Forceps
19	i	3,445	13	34	4	27	Forceps
33	iv	4,290	4	20	11	28	Forceps
22	i	3,740	13:30	55	5	16	Forceps
35	iii	3,060	2:15	12	13	18	
28	v	4,250	1:40	18	2	32	
28	ii	3.530	10	50	6	21	Forceps

Total 21

The results are summarized in Tables I, II, and III. For those who may be interested, Group D is given in detail. The number of babies weighing over 4,000 Gm. average about the same in Groups A and B, at about 10 per cent. In Group C the percentage is raised to 15 per cent and in Group D to 33 per cent. It is true, therefore, that babies carried past the expected term are larger. Most of the babies weighed from 3,000 to 4,000 Gm. (151). There were 5 babies who weighed less than 2,500 Gm. Only one baby weighed more than 4,500 Gm., a percentage of 0.5 which compares with Koff and Potter's findings of 194 per cent in 20,219 deliveries at the Chicago Lying-in Hospital.

6. As you can see by the table, there is a wide variation in the weights of babies delivered by normal women. The most marked difference was in the group of patients who delivered from seven days before term to term. Here the smallest baby weighed 1,814 Gm. and the largest 4,400 Gm., and no mistake was made in the reckoning by the patient or the physician. The pediatricians who examined the large babies hesitated to say definitely that any of them were postmature.

There was no fetal or maternal mortality in this series, and, so far as I know, all the babies are alive and well at this time.

The number of forceps deliveries is high since nearly all of these patients were delivered under analgesia and were not cooperative in the second stage of labor.

From observation and a review of this series, I firmly believe we are not justified in interfering with the natural processes of pregnancy and labor in normal women. I protest against such a procedure.

122 SOUTH MICHIGAN AVENUE

DISCUSSION

DR. JOHN H. MOORE, GRAND FORKS, N. D. (By Invitation).—Dr. Cornell has pointed out that we have no accurate criteria by which we can determine the weight of the baby in utero or the presence of postmaturity. To that might be added that we do not know what institutes the mechanism of labor. When we attempt to induce labor by medical or mechanical means, we are attempting to set in motion a force whose effectiveness is not predictable with any degree of accuracy. Two cases illustrate the problem:

CASE 1.—A multiparous patient, gravida v, para iii, entered the hospital on May 9, 1940. Her estimated date of confinement was May 14. She was not in labor and came to the hospital solely because of a feeling that labor was imminent. Her condition was entirely normal, and upon rectal examination, the cervix was found to be completely effaced, the os dilated to 4 cm. and the head engaged in occipitoanterior position. I ordered one ounce of castor oil, to be followed one hour later by a tap water enema and three minims of pitocin by hypodermic injection. Forty-eight minutes after the pitocin had been given she delivered a baby boy weighing 3,960 Gm. During the third stage, which lasted eight minutes, she lost 400 c.c. of blood, due to the fact that the placenta separated but became constricted by the contracted cervix. Following the removal of the placenta, she had an additional blood loss of 500 c.c., making a total blood loss of 900 c.c. This patient illustrates the unusual violence which may characterize the onset and course of a labor which has been induced by the most common medical measures.

CASE 2.—In contrast is the case of another multiparous patient, a gravida ii, para i, upon whom I also induced labor for convenience. Her previous labor, conducted elsewhere, had lasted forty-eight hours and was terminated by a forceps delivery. Her estimated date of confinement was July 17, 1940, and she entered the hospital on July 19, 1940. Her pregnancy also had been entirely normal and she was in excellent condition. The cervix was soft, one half effaced, the os was dilated to 2.5 cm., and the head was engaged in occipito anterior position. Induction of labor was attempted with castor oil, enema and pitocin. Twenty-four hours later, these measures having failed, the membranes were ruptured artificially with the resulting discharge of a large amount of liquor amnii. *Nine days later* labor began and, after a first stage of fifteen hours and a second stage of fifty-two minutes, the patient delivered a normal baby girl weighing 4,680 Gm. The blood lost was 30 c.c., and there were no puerperal complications.

Here are two cases of induced labor in normal pregnant women at term, induced, theoretically, for the patients' convenience. The violent onset of labor in one, with the complication of postpartum hemorrhage, and the latent period of nine days in the other, with the membranes ruptured, made me wish that I had not induced either.

I will admit that one may review large series of cases where labor has been induced on normal pregnant women, with no apparent complications in either the mothers or their babies; but if pregnancy and labor are still to be regarded as normal physiologic processes, the burden of proof for the safety, the efficiency, and the wisdom of the induction of labor in normal pregnant women is directly the responsibility of the obstetrician who presumes to interfere with these natural processes. As I get older, I find myself less willing to assume that responsibility, even though many of my patients live in towns without hospital facilities and often in communities where medical attendants are not readily available. When I do assume that responsibility, as in the cases mentioned, I feel that I have let expediency overrule obstetric judgment.

DR BUFORD G. HAMILTON, KANSAS CITY, MO.—Dr. Henry Schwarz and those outstanding leaders of his time always taught and practiced that if women were left alone they could and would have their babies. They also advocated that the membranes were for the protection of both the mother and child. Sad experience has taught me how wise these fundamentals are today.

The changes in the lower uterine segment and cervix are important to note in the last weeks of pregnancy. As I have watched these phenomena, I am

convinced that if there is any evidence that justifies the assurance that a patient is due or near term it is the preparation of the lower uterine segment and cervix. Most often labors are longer and more complicated where these signs are not present. Premature labor from whatever may have been the cause with inductions, especially in primipara, are too often long, tedious, and difficult. These observations cause us to reason that if the lower uterine segment and cervix are prepared for labor, an induction is contraindicated other than for definite reasons; also if the lower uterine segment and cervical preparation is not present, the hazards are too great to warrant interference.

May I suggest these observations for your serious consideration since, if this reasoning is true, there can be no reason for the induction of labor other than for definite indications.

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—As Editor of your official source of publication I sometimes have a feeling of doubt and hesitancy about having included in our pages so many papers dealing with routine induction of labor. We try to be catholic, but I feel a hesitancy in accepting papers of that type, especially when we have reports of series of several hundred cases in routine obstetric practice where labor has been induced, often without any regard to the condition of the cervix.

I do not agree with Dr. Cornell as to all of his restrictions, because some women require an induction of labor who are only a little bit removed from the normal. But in consenting to do that you must have certain conditions present, of which the principal one is a normally prepared cervix.

DR. ALBERT W. HOLMAN, PORTLAND, ORE.—In 1936 my late Associate, Dr. Mathieu, gave our results in 750 inductions of labor. At that time he spoke of our induction routine, and I think a great many men misunderstood him and thought he said routine induction. Our inductions are not routine. I am making no plea for routine induction of labor but would like to give a few of our results in our series which now amounts to 1,163 cases. Our corrected fetal mortality is 0.7 of 1 per cent; our maternal mortality is 0.3 of 1 per cent. We have had one case of prolapsed cord and no case of separation of the placenta in this series.

I would like to ask Dr. Cornell what type of induction he does. The type that Mathieu advocated was medicinal induction of labor, and he always stressed the point that the membranes should never be ruptured until the cervix was effaced.

DR. H. B. VAN WYCK, TORONTO, CANADA.—Do not all the considerations that Dr. Cornell has brought forward to contraindicate induction of labor in normal cases apply equally well to the effort that is made to escape borderline disproportions by premature induction of labor?

DR. A. J. RONGY, NEW YORK, N. Y.—Modern contraceptive methods and the practice of birth control have thrown a new light on the traditional term, "overdue," in the practice of obstetrics. A great many intelligent women now know exactly when impregnation may have taken place. The last date of menstruation is no longer a true criterion upon which the duration of pregnancy can be predicted properly. I have a series of patients whose calculation for the possible onset of labor were more correct than mine, because they knew actually when pregnancy might have ensued. Their date for labor was usually ten to fourteen days later than the established obstetric calculations would indicate. Therefore, in many cases the onset of labor is delayed, not because the woman is actually "overdue," but because pregnancy took place approximately close to the menstrual period.

I have never induced labor for the convenience of the patient or myself. That is definitely meddlesome obstetrics. The expert obstetrician may at times induce labor at an appointed time and not run into any untoward complications, but should this method become a recognized obstetric procedure, it would cause the death of many mothers and babies. The only indication for induction of labor is when the pregnancy becomes dangerous to the mother and rarely when the child becomes oversized. However, the weight of the patient must be carefully watched in all

women who are thought to be "overdue." Given a patient who is "overdue," who begins to lose weight, though she may not have any other constitutional disturbances, this to me is always a danger signal for both mother and child, and may be a proper indication for induction of labor.

DR. IRVING W. POTTER, BUFFALO, N. Y.—Owing to certain procedures that we have carried on in our office for a number of years, with satisfaction to our patients and ourselves, we have never had to induce labor, and when we talk about it, we only do so to condemn it. Whether it is done by medicinal or other means, we look for the effacement of the lower uterine segment; we talk about that in preference to dilatation of the cervix and do not speak of that any more.

We do not schedule our cases either, but we deliver them at a fairly reasonable time. I simply wanted to get our position straight in the eyes of some people by saying that although we do deliver our patients at a certain time, we never induce the labor.

DR. E. L. CORNELL (closing).—I stressed the fact that this paper was devoted exclusively to the normal pregnant woman and not to cases of disproportion, the toxemic, etc. I desired to bring out the fact that women do go well past term, as we compute it, and still deliver babies that are normal.

In the entire series, there were no babies lost, no prolapsed cord, and no mother died. So far as I know, all of the babies are still living. This series only goes back about two and one-half years.

I did not say anything about the types of induction because there were so many different types utilized that it would have been necessary to take up each individually.

I recall very distinctly a woman who delivered the largest baby at the Lying-in Hospital at the time I was on the attending staff. It weighed 14 pounds and she delivered it in two or three hours.

PUBERTAS PRAECOX DUE TO OVARIAN TUMORS*

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(From the Philadelphia Lying-In Hospital)

ONE of the most intriguing phases of gynecology from the pathologic, endocrinologic, and clinical viewpoint, is the study of so-called "unusual tumors of the ovary." As early as 1895, Von Kahlden reported a patient with "adenoma of the Graafian follicle with transition to carcinoma." It has been generally agreed that this was probably the first authentic case of granulosa cell tumor. In 1914, Von Werdt described a tumor of the ovary as a granulosa cell type, but it was not until 1931 when Robert Meyer reported 33 such cases that interest in investigation of these tumors was stimulated. As a result, innumerable papers have been written on these and other neoplasms of various glands, such as the adrenal and pineal, which cause unusual disturbance of the normal female function. In spite of the fact that there are still many points in connection with these tumors which have not been generally agreed upon, the information which is available gives us a very much clearer concept of these conditions. It is not my desire to attempt to review completely the medical literature nor to dis-

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cuss all of these unusual tumors but rather to confine my discussion to the so-called granulosa cell tumors of the ovary and report two cases of precocious puberty.

Granulosa cell tumor can no longer be considered a rare neoplasm. However, because of the confusion in classification of the earlier cases reported, it is almost impossible to estimate accurately its incidence. As general interest in these neoplasms increases, the incidence seems to increase.

Since 1931 there have been many compilations on this topic, including a very masterful Monograph by J. Varangot, which is probably one of the most complete dissertations available on this subject. In their review of 160 granulosa cell tumors, Bland and Goldstein, in 1935, stated that 85 others had been reported previously, making a total of 245. In 1937, Pratt collected about 200 cases. Novak and Fauvet considered that granulosa cell carcinoma is a fairly common tumor which comprises about 10 per cent of all solid malignant ovarian neoplasms. They have studied 75 such neoplasms in their own laboratory. Recently Traut and Marchetti made a preliminary report on 61 ovarian tumors belonging to this class of neoplasms, which were collected from a group of New York hospitals.

A granulosa cell tumor may be present at practically any age. The incidence of occurrence before puberty, however, is very small.

In 1934, Bland and Goldstein collected 8 cases which occurred under the age of 11 years. Gross in his recent article states that there are 11 case reports of patients under 10 years and reports one occurring at 13 months. Up to the present time I believe that to be the youngest patient reported. Schulze in her discourse on granulosa cell tumors stated that in all probability the total number was 14. She did not include the case reported by Mannheimer of Stockholm nor Gross' recent report, so that actually 16 cases of ovarian tumors have been reported in very young children who have shown signs of precocious puberty.

The histogenesis of sex cell tumors of the ovary remains a controversial subject. The older theory that the granulosa cells were derived from the germinal epithelium has been more or less discarded by the later theories of Fischel and Meyer.

Most writers today agree that granulosa cells arise from the ovarian mesenchyme. Novak in his recent book on obstetric and gynecologic pathology, states that there is reason to believe that the histogenesis of these feminizing tumors may be traceable to a very early progranulosal, prothecal phase of development. Both the granulosa and the theca are derived from the ovarian mesenchyme, and therefore the feminizing tumors may develop with granulosal or connective tissue characteristics. Supporting this mesenchyme theory are cases reported by Klaften, Rummeld, and Compton. Recently Norris and Dunne reported a case in which a retroperitoneal recurrence was noted a number of years after the original operation for granulosa cell tumor. Voigt reported a case of primary giant granulosa cell tumor of retroperitoneal origin in a woman of 51 years of age who three years previously had undergone a supravaginal hysterectomy for a myoma. At the second operation the ovaries were found to be normal senile organs, and a large retroperitoneal granulosa cell tumor with extension into the mesosigmoid was removed. Novak concludes that both the granulosal and the thecal tumors should be included under some such designation as feminizing mesenchyma of the ovary. He also believes that the luteoma of the ovary represents merely a luteinized granulosa cell tumor.

Furth and Furth have made a very extensive report on their work with x-rays on mice, based on the probability that these neoplasms can be induced by general irradiation. Norris and Dunne conclude from their review that irradiation plays little, if any, part in the production of these tumors.

From a gross pathologic standpoint, granulosa cell tumors assume a variety of appearances, depending upon their size and type. Some are soft and cystic while others are semisolid or solid, depending upon the amount of tumor tissue undergoing necrosis and resulting in the formation of cystic space. It may be generally stated that it is an ovoid, solid, small, encapsulated, firm neoplasm. There is nothing characteristic in the gross appearance whereby one may know that he is dealing with a definitely malignant type of granulosa cell tumor, unless peritoneal metastasis or spread to other pelvic organs is found at operation. There is also a variability in the microscopic pattern. Novak believes that this is chiefly responsible for the confusion of nomenclature and classification of a considerable number of ovarian tumors which are now accepted as having a common histogenesis from granulosal or progranulosal tissue. The variability is exhibited not only in different tumors but in one and the same tumor, in different parts. It therefore becomes important to study numerous blocks in order to derive an intelligent impression of the tumor as a whole. Granted that numerous histologic patterns may be seen in the same tumor, one cell pattern usually predominates. The main histologic types have been described in detail by numerous authors as follicular, cylindromatous, trabecular, and diffuse.

Malignancy is still a moot question in the study of these tumors. The tumor is often called granulosa cell carcinoma and yet Karsner states that even the most gloomy statistics, unlike the data of other internal carcinomas, admit of cure in 62 per cent of the cases. He also states that it is not good practice to consider a tumor malignant merely because of its potentiality, and no more justifiable to call all granulosa cell tumors carcinomas than to classify under this same heading the mammary adenoma, the papilloma of the bladder, and other similar lesions.

In a follow-up study of 32 cases by Novak and Brawner, the clinical malignancy rate was 28.1 per cent. Huckel reports a case under observation for a period of fourteen years after operation. During this time the patient remained well and then developed a pelvic recurrence which was adherent to the uterus and small intestines. The uterus, right tube and ovary, and tumor were removed, followed by x-ray therapy. Six weeks later the patient developed a second recurrence at the root of the mesentery in the left upper abdomen, with involvement of the intestines and abdominal wall. Norris and Dunne recently reviewed a series of 24 patients treated at the University of Pennsylvania. Of these 24 patients, 10, or 45.8 per cent, survived and except for 1 patient with retroperitoneal recurrence, all have remained well varying from a period of two to twenty-two years. Seven, or 29.2 per cent, died, with death resulting in every case from known malignancy. One patient died five years after treatment from an unknown cause. Six patients have been lost. If these 6 patients are included as having died from the effects of granulosa cell tumor, the clinical malignancy rate would be 54.2 per cent which is much higher than is ordinarily attributed to these neoplasms. Norris and Dunne conclude that the granulosa cell neoplasm should not be considered too lightly with regard to the degree of malignancy. The pendulum seems to be swinging toward the malignant side after a period, during which these tumors were becoming more and more to be considered nonmalignant. The importance of the question of malignancy seems to lie in the fact that although ordinary ovarian carcinoma recurs within the first year, there are numerous cases of recurrence of these tumors many years after the original operation. It seems likely, therefore, that as in many other tumors the

grades of malignancy have to be considered, although Novak believes that it is not as yet possible to base these on histologic criteria. Postoperative deep x-ray therapy is not universally considered a necessity. Many feel that x-ray therapy should be reserved for the treatment of recurrence, as it is a well-established fact that the granulosa cells are quite radiosensitive. In this way the patient's tolerance for deep x-ray therpay is maintained at its maximum and treatment can be concentrated over a limited area.

Accurate hormonal studies on these tumors are still relatively infrequent. This is probably due to the fact that the diagnosis is made only on pathologic examination when it may be too late for hormonal studies to be of value.

Schulze states that the standards for quantitative estimation vary so that attempts at comparison are very confusing. Palmer in his recent study of a tumor occurring in a 19-year-old girl also called attention to this problem. Mannheimer in the report of a granulosa cell tumor in a 4-year-old girl attempted to make a more thorough research on the hormones of the granulosa cell tumor by making a preparation of an extract of the tumor for a series of tests on animals. Unfortunately these could not be accomplished as it was impossible to produce an effective extract. In his case, the Zondek-Aschheim reaction was negative, and the percentage of prolan in the urine was extremely insignificant. He did, however, implant one-tenth of a gram of the gland in the femoral muscles of mice which resulted in one of the animals reacting positively, and states that this may be an evidence of the fact that the tumor in question contained folliculin in greater or smaller quantities. In the case reported by Bland and Goldstein, the estrin pregnancy test was positive two days prior to operation, while the Zondek-Aschheim test was negative. Seven days postoperatively, estrin was absent. When this tumor recurred two and one-half years later in the remaining ovary, estrin was found in the blood and urine preoperatively, and the Zondek-Aschheim reaction was also positive. It is interesting to note that in the recent case report by Gross, in the follow-up six months after removal of the tumor, it was found that a twenty-four-hour specimen of urine contained 48 international units of estrogen. The breasts and the labia had regressed almost to normal size, and the pubic and axillary hair had disappeared. There was no evidence of recurrence by physical examination, and it was felt that the relatively high excretion of estrogen for a child of this age probably resulted from recurrence of the neoplasm. Pelvic exploration was therefore advised and undertaken but no recurrence was demonstrated. The uterus, also, had returned to normal size. The work of Strong, Gardner, and Hill with a transplantable granulosa cell tumor of the mouse is of especial importance. In the female hosts of the transplant there was continued estrus which disappeared after removal of the tumors. Karsner concludes that granulosa cell tumors produce estrogenic substance and quotes many case reports, but as to the continuity, the rhythm, or amount, no conclusion can be reached. He also states that it cannot be definitely said whether the condition is due to hyperestrinism or dysestrinism. Further hormonal studies with a more accurate standardized technique as advocated by Palmer should and undoubtedly will be forthcoming.

The clinical characteristics, as in other ovarian neoplasms, depend upon whether they are large enough to cause pain and discomfort. The more distinctive symptomatology is dependent upon the capability of the tumor cells to produce the estrogenic hormone. During the female reproductive period, because the secondary sex characteristics have long since been developed, there is no definite change, and the tumor merely adds quantitatively to the cyclical hormonal content of the blood. Tumors occurring during the postmenopausal age, when very little estrogenic hormone is found in the blood, produce re-establishment of periodic menstruation-like bleeding and also hypertrophy of

the uterus. There is no demonstrable effect upon the secondary sexual characteristics. This is probably due to unreceptivity during this period. With removal of the tumor at this age, the abnormal menstruation ceases. Novak and Dworzak observed a patient who experienced a second menopause from the standpoint of vasomotor phenomena after removal of the growth. When these tumors occur during childhood, before inauguration of the normal estrogenic function, the clinical manifestations of precocious puberty are evoked; namely, precocious menstruation, hypertrophy of the breasts, the appearance of axillary and pubic hair, development of the external genitalia, and in most instances, hypertrophy of the uterus. Removal of the tumor, whether it be primary or recurrent, is followed by regression of all of these symptoms.

Novak points out that the precocious menstruation of this syndrome is an anovulatory, purely follicular type, in which respect it differs from certain other types of precocious puberty and menstruation, in which ovulation and menstruation occur. In the latter group insemination might theoretically bring about fertilization at an abnormally early age. Mengert reported an ovarian cyst which histologically appeared to be a follicular cyst, causing precocious sexual development in a child 5 years of age in whom the infantile state was resumed following operation. The pathologic discussion and photomicrograph showed no resemblance to a granulosa cell tumor.

On the other hand, granulosa cell tumors have been reported which have produced no vaginal bleeding in spite of a marked increase in estrogenic excretion. It can definitely be stated that the presence of precocious puberty with a definite ovarian enlargement is strongly suspicious of a granulosa cell tumor. During active sex life the bleeding may be present only in the form of irregularity of the menstruation so that the preoperative diagnosis can only be suspected. In the postmenopausal state, the recurrence of vaginal bleeding associated with an adnexal mass should make one at least suspicious of a granulosa cell tumor.

During the past year there have come under my observation two children, one at 9 months and one at 22 months, who had the above mentioned symptoms. Inasmuch as the first child was 4 months younger than the youngest case reported to date, and in the second child a diagnosis of granulosa cell tumor was made which proved to be a simple follicular cyst of the ovary, I should like to report these two cases in detail.

CASE 1.—G. K., 9 months of age, was referred by Dr. John Williams and Dr. William Danehower. Chief symptom was intermittent vaginal bleeding for two months, excessive growth of hair, and a lump palpable in the left abdomen. Family history was negative, there being one other apparently normal child two years older. This patient was born spontaneously. At birth she weighed 6 pounds 8 ounces and was perfectly normal, except for excessive and luxuriant growth of hair on the head, reaching almost to the shoulders. She was artificially fed without difficulty. At the age of one month she weighed 7 pounds 11 ounces and measured 27½ inches in length, was very active for her age, and her head was still covered by a dense crop of thick black hair. When she was approximately 7 months old the mother noticed some vaginal bleeding. This consisted only of spotting sufficient to cover an area about the size of a dime. Coincidental with bleeding, the mother noticed that the breasts would enlarge and the child's disposition would change. Instead of being happy and active, as usual, the patient would become irritable and restless. After

cessation of the bleeding, the engorgement of the breasts would subside and the child's disposition would revert to a happier mood. Six weeks later the bleeding recurred. This period was of four days' duration, during which time a small amount of spotting occurred each day. In the interval between the periods of bleeding, a white vaginal mucous discharge was present. About this time the mother noticed a small amount of pubic hair which seemed to be definitely increasing in amount. Because of a cold, the patient was seen by the family physician, who, because of the existence of the pubic hair, made a rectal examination which revealed a mass about the size of a plum in the lower abdomen. The child was then admitted to the hospital for study. Examination on admission revealed, in addition to the enlarged breasts and pubic hair, some hypertrophy of the vulva. There was also a slight vaginal mucoid discharge. The following are the results of the studies made: The glucose tolerance curve seemed to be within normal limits. The Friedman test was negative. The urine was negative. X-ray of the head and long bones by Dr. Paul Bishop showed them to be entirely within normal limits. Study of the ossification centers showed normal development for a child of this age. The blood count was as follows: Hemoglobin, 71 per cent; red blood cells, 4,710,000; white blood cells, 8,700; differential count: polymorphonuclear leucocytes, 20 per cent, lymphocytes, 79 per cent, monocytes, 1 per cent. Hormonal studies made by Dr. Abraham Rakoff in the Research Endocrinological Laboratory, Department of Obstetrics, Jefferson Medical College Hospital, showed the following results: Sept. 5, 1939, Serum estrogen (Fluhmann), 6 to 9 mouse units per 100 c.c.; quantitative urine estrogens, 66 mouse units per twenty-four hours; serum gonadotropins, mouse units per 100 c.c., none demonstrable; quantitative urine gonadotropins, international units per twenty-four hours, none demonstrable. A tentative diagnosis of granulosa cell tumor of the left ovary was made.

On Oct. 25, 1939 operation was performed under open drop ether anesthesia. A left paramedian incision was made approximately 2 inches in length. Upon exposing the peritoneal cavity, a tumor, which proved to be the left ovary, was brought into view. The uterus was thought not to be enlarged. Inspection of the right tube and ovary showed no abnormality and the right ovary seemed to be normal in size. A left salpingo-oophorectomy was performed. Patient reacted nicely and made an uneventful recovery. She was discharged from the hospital on the eighth postoperative day.

The specimen was sent to the Ayer Clinical Laboratory of the Pennsylvania Hospital for examination and the following is the pathologic report as submitted by Dr. John Bauer, Director:

Specimen 29271.—Gross: The specimen was that of fresh tissue about 4 by 3.5 by 2 cm., somewhat ovoid in appearance. At one pole a small tortuous salpinx was attached, suggesting therefore that the mass was an ovary. The entire surface was thin, smooth, and glistening. A few small translucent cysts projected outward like small shallow vesicles, and a larger one having a blue color was noted below the surface. The vessels were not injected. Shining through the surface, the yellow color of the tissue within could be seen. On gross section no recognizable ovarian tissue could be seen. All appears to be replaced by a golden yellow tissue having an irregular lobular arrangement separated by strands of grayish white stroma and a few thin-walled cysts filled with clear slightly brown-tinged fluid. Microscopically: There were a few premordial follicles in the cortex of the ovary which was extremely narrow and surrounded the tumor. The tumor for the most part consisted of regular, small, polygonal or oval cells with even, regular, oval, vesicular nuclei, some in division. These cells appearing like granulosa cells formed a variety of patterns, some solid, some cystic. Surrounding the nodules of granulosa cells was a loose stroma of connective tissue which was reticular and traversed by a number of small, delicate capillaries and contained cells with small deeply-staining oval nuclei which were scattered throughout, chiefly at the periphery in small groups of four to a dozen or more. They suggested a derivation from the granulosa cells, comprising the main tumor but which had become separated and compressed in their extension beyond the main tumor. In other fibrous areas where these small cells were not as numerous, the connective tissue stroma appeared somewhat more condensed and apparently older. Different areas of the tumor showed a diffuse variety, a finely

folliculoid pattern, and in places a cystic pattern. Call-Exner bodies were seen chiefly in the finely folliculoid areas and in the diffuse areas. A considerable amount of lipoid was present in the granulosa cells and in the cells extending into the loose stroma surrounding the typical granulosa cell areas. The appearance of the tumor suggested the development of follicles and their attempted transformation to corpora lutea and finally to corpora fibrosa. Malcolm Dockerty and Emil Novak concur in the diagnosis of granulosa cell tumor of the ovary.

Patient's progress following operation showed a very rapid return to normal. The pubic hair disappeared, the breast engorgement subsided, and there was much less vaginal secretion. For two or three months following operation, at approximately twenty-eight-day intervals, the child became slightly irritable and had attacks of nausea. There were no other signs or symptoms of menstruation. Six months following operation further hormonal studies were made by Dr. Rakoff with the following result: May 15, 1940, Serum estrogen (Fluhmann), mouse units per 100 c.c., none demonstrable; quantitative urine estrogens, mouse units per twenty-four hours, none demonstrable; serum gonadotropins, mouse units per 100 c.c., none demonstrable; quantitative urine gonadotropins, international units per twenty-four hours, none demonstrable.

This patient was seen within the last month and seems to be well in every respect. There have been no further signs of recurrence either in symptoms or upon physical examination.

CASE 2.—C. G., 22 months of age, was referred by Dr. Ralph M. Tyson, who first attended the child when she was three weeks old. Her birth weight was 7 pounds 6 ounces. She was seen at irregular intervals during the following year and from the age of 7 months until 14 months, no medical attention was required. At fourteen months of age, she weighed 23½ pounds and was in an excellent state of nutrition. She could sit, stand, walk with help, and was alert and happy. It was at this time that enlargement of the labia and the presence of pubic hair was first noticed. Upon rectal examination it was thought that the left ovary was enlarged to about the size of the end of a thumb. There were no breast changes demonstrated. In January, 1939, the mother noticed some vaginal discharge and some blood in the urine. Urinalysis at that time revealed the presence of red blood cells. Because there had been no rapid progress in development of the secondary sex characteristics, she was kept under observation until November, 1939, when, at the age of 22 months, she was referred to me for examination. The mother stated that when the child was 17 months of age she was more restless and irritable that usual. This period of irritability which occurred in June, persisted for three days, after which time the patient seemed better. Again in August and September the patient underwent two successive periods of restlessness and irritability, during which time blood was again noticed in the urine. There had been very little development of the breasts and no increase in the amount of pubic hair. Rectal examination revealed a definite enlargement of the left ovary. The following are the results of the studies made after admission to the hospital for observation: The glucose tolerance curve was normal. Friedman test was negative. The urine was negative. The blood count was as follows: Hemoglobin, 72 per cent; red blood cells, 4,290,000; white blood cells, 5,200; differential count: polymorphonuclear leucocytes, 37 per cent; lymphocytes, 61 per cent; monocytes, 2 per cent. X-ray of the pituitary showed no evidence of abnormality, and the long bones were normal. Intravenous urography showed both sides of the urinary tract visualized, and no evidence of any gross defect present. Hormonal studies made by Dr. Rakoff showed the following results: Nov. 6, 1939, serum estrogen (Fluhmann), mouse units per 100 c.c., none demonstrable; quantitative urine estrogens, mouse units per twenty-four hours, none demonstrable; serum gonadotropins, mouse units per 100 c.c., none demonstrable; quantitative urine gonadotropins, international units per twenty-four hours, none demonstrable. A tentative diagnosis of granulosa cell tumor of the left ovary was made and operation advised.

On Nov. 15, 1939 operation was performed under open drop ether anesthesia. A left paramedian incision was made with exposure of the peritoneal cavity, revealing an enlargement of the left ovary, part of which was a very thin-walled cyst. The uterus was not perceptibly enlarged and the right ovary seemed to be normal.

A left salpingo-oophorectomy was performed. This patient made an uneventful recovery and was discharged from the hospital on the tenth postoperative day.

The specimen was sent to the laboratory for examination, and the following pathologic report was submitted by Dr. Bauer: Specimen 29395.—Gross: The specimen in formalin consisted of a small 3 by 1 by 1 cm. fragment of ovary which contained many small cysts filled with a clear fluid. One end of the ovary was missing, this having been removed for experimental purposes. Microscopically: Near the surface were a number of immature ovules such as one sees in infants and young children. Deeper in a somewhat loose stroma were a number of cystic follicles lined by small round oval cells, suggesting granulosa cells which were heaped up in one area to form a mound in the depths of which was a tall oval granular space suggestive of an ovum but not surrounded by a zone pellucida or containing any other nuclear material. This mound of granulosa cells was suggestive of a cumulus oophorus and not suggestive of a granulosa cell tumor. There was no evidence of luteinization in any part of the section. Neither was there any evidence of a granulosa cell tumor. A low power photograph showed the cystic nature of the tumor, and a higher power photograph showed the small area of granulosa cells, suggesting a maturing Graafian follicle. On Dec. 8, 1939 Novak saw this section and said that the tissue was that of a normal ovary. Our diagnosis was ovary with follicular cysts. Fron the histologic appearance, it is difficult to interpret the clinical picture. I do not recall another instance of this lesion in our files and would like to hear more about the outcome of this patient.

Part of the cystic portion of the ovary was imbedded in the muscles of mice but the results were negative. During the last ten months the child seems to have been perfectly normal with no recurrence of periods or irritability. The pubic hair has entirely disappeared and although the breasts were not markedly enlarged, there seems to have been a decrease in their size.

SUMMARY

Two cases of ovarian tumors associated with precocious puberty are reported in this communication. The one tumor is what we consider to be a typical granulosa cell tumor, the other is a simple follicular cyst of the ovary. The fact that the second case responded to operative procedure and returned to normal infantile type would lead one to believe that surgery is indicated in these ovarian tumors, even though they are not of granulosa cell type.

From a review of the literature and a study of these two cases, I have no doubt that important advancements will be made, particularly with regard to the hormonal studies of this group of neoplasms.

Functioning tumors of the ovary which were formerly unrecognized, today represent a subject of such broad possibilities as to be of interest to the medical profession in general. From an endocrinologic viewpoint, these tumors furnish definite evidence of hormonal production and its clinical effects. To the embryologist, the various phases of cellular differentiation are of especial interest. The identification of these "unusual tumors" stirs the interest of the internist. The pathologist's, as well as the surgeon's, interest is concentrated upon the difficult problem of confirming the clinical diagnosis and choosing a proper course of treatment. The general interest in the study of these tumors has been stimulated to such a degree that a positive diagnosis is more likely in the majority of cases. Consequently, through proper diagnosis, pathologic confirmation and proper treatment, the prognosis today is more favorable than in the past.

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DISCUSSION

DR. JAMES E. DAVIS, Ann Arbor, Mich.—Studies of pubertas praecox are limited at present to the effects produced on tissues and genital functions. The cause or causes of the hormonal imbalances are not sufficiently understood.

By accepting the origin of granulosa cell tumors as arising from the undifferentiated ovarian mesenchyme, this structure is made responsible for both stromal and follicle cells of the ovary. Functionally the mesenchyme of the ovary is cytologically sexually determined. The inherent potency is directed to utilize granulosa cells as typical feminine functioning units.

Malignancy doubtless occurs in 25 to 30 per cent of granulosa cell tumors as at present diagnosed. If the life history of all cases were completed and tissues then examined, a higher rate would doubtless prevail.

There is no reason why granulosa cell tumors should not present structural stages of malignancy similar to all other tumors and consequently be credited with unripe, midripe, and ripe cell types. This would simplify the classifications.

DR. H. M. N. WYNNE, Minneapolis, Minn.—If granulosa cell tumors could be transplanted or reproduced in experimental animals, it would be possible to test the effect of hormones antagonistic to estrin. We might also gain more knowledge of the factors involved in the growth of rests.

Dr. Lull states that in his second case hyperestrinism was not demonstrated. That portion of the ovary not examined histologically was used experimentally with negative results. Might not a very small granulosa cell tumor have been overlooked in that part of the tissue?

I have observed but one case of precocious puberty which occurred in 1916. She was a negro girl, 7 years of age. A solid tumor of the ovary was removed and a diagnosis made of carcinoma of the ovary. Several months after the operation the secondary sexual characteristics had regressed almost completely. I think this was almost certainly a granulosa cell carcinoma.

I believe our studies of the several unusual ovarian tumors might be helped by a national registry. The follow-up data over a period of years would certainly expedite our collection of facts and give us more certain knowledge of what to expect after the removal of such tumors.

DR. JOE V. MEIGS, Boston, Mass.—At the International Congress on Cancer held in Atlantic City last fall Novak and Machado both read papers on granulosa cell tumors. It was the opinion of most men at that meeting that it is a rather rare tumor, but Novak thought they are very common. I believe they are not very common. I have had but one case.

At that meeting Machado talked about how to differentiate between the granulosa cell tumor, granulosa cell hyperplasia, and the theca cell tumor. These conditions do not occur alone, but each case is almost always a combination.

Two conditions have not been spoken about that produce precocious puberty, which in my experience are more common than the granulosa cells. At our hospital there have been several cases with lesions of the hypothalamus. I have recently had one in a girl who at the age of one and one-half years menstruated regularly. At the age of 3 she was so large that she had to go to school with children 5 years old. At the age of 10 she had stopped growing and the other children her age were a half head taller than she was. Now she menstruates perfectly regularly, and her condition is satisfactory in every way. Her lesion was probably of pre-pituitary or hypothalmic origin.

Then we must never forget Albright's work on early developed children who have brown spots, bone cysts, and precocious puberty. He has now collected 14 or 15 of these cases. It would be interesting to know whether the second case reported this morning had any brown spots, although her bones were x-rayed and were said to be negative. I understand that Albright has written to inquire about the child who gave birth to a baby in South America at the age of five and has been informed that that child has brown spots and bone cysts.

DR. FRANK R. SMITH, NEW YORK, N. Y.—At the Memorial Hospital we have had only 16 of these patients with granulosa cell tumors. With one exception, they had all had previous operations before coming to the hospital. I have recently had an opportunity to see a patient who five months ago was treated by the million volt x-ray machine over the tumor mass, which seemed to regress. Then a month ago I re-operated upon this patient and found not only actively growing tumor but little evidence of radiation reaction on the granulosa cell tumor. There was fibrosis of the tissue surrounding the tumor. Does Dr. Lull know of any evidence of radiosensitivity in these tumors?

DR. LULL (closing).—There was no perceptible enlargement of the uterus in either one of these cases. In women, particularly after the menopause, who have granulosa cell tumors, the diagnosis is suspected preoperatively by the fact that there is enlargement of the uterus.

This patient about whom Dr. Meigs inquired had no brown spots.

It is perfectly possible in the second case that the part of the tumor which was not examined microscopically may have had some evidence of granulosa cell tumor. The symptoms were so similar that preoperatively I felt quite certain that the second patient had a tumor of the left ovary which would prove to be of granulosa cell type.

ACTINOMYCOSIS OF THE OVARY*

W. A. Coventry, M.D., Duluth, Minn.
(From The Duluth Clinic)

ON Nov. 14, 1938, Miss E. B., aged 20 years, consulted me, giving the following history:

The family history was negative. There had been no previous illness except three years prior to this time when she had had an attack of pain in the lower right quadrant which lasted for two weeks. There was fever; she was observed at her local hospital and treated expectantly. In the three-year interim she had been very well. Her present complaint was that seven days previously she had had a pain in the lower right quadrant of the abdomen, radiating into the right groin, not related to the menstrual period. At this time she vomited. She was transferred to her local hospital (in another city) and was under observation for three days. There was no particular abdominal tenderness. Her temperature was 101° F. but fell to normal the next day. The pain promptly disappeared and she was sent home. Three days later the pain reappeared and she came under my observation. The pain was intermittent in the lower right quadrant of the abdomen. It was associated with loss of appetite. Constipation had been the rule.

At the time of our first observation, the blood pressure was 104/60. Except for a leucocytosis of 28,700 the blood counts were essentially negative. The urinalysis was negative. The blood Wassermann was negative. The heart and lungs were normal to auscultation and percussion. There was some slight tenderness in the lower right quadrant of the abdomen. There was no rebound tenderness, and it was not suggestive of an abscess or appendicitis. Bimanual examination revealed the uterus in good position and normal size. In the right adnexa one could feel a mass which was diagnosed as a possible pus tube. Smears for Neisserian organisms were negative, and possible exposure was denied.

She was referred to St. Luke's Hospital for further observation and on Nov. 21, 1938, she was operated upon by me. Upon opening the abdomen there was a peculiar odor, suggestive of colon, but not typical. Further examination revealed a pelvic inflammatory mass involving the right tube and ovary. The left tube and ovary were normal. The sigmoid and cecum were normal. The gall bladder was negative to palpation. The appendix was postperitoneal, lying in the midline. The uterus was also normal in size and negative for tumors. It was felt that the mass on the right side was a tuboovarian abscess. The mass which included the tube and ovary was removed without breaking into the capsule. The appendix was removed in the usual manner. The patient made an uneventful recovery with primary union. She was discharged fourteen days later.

The report of the pathologist, Dr. A. H. Wells, was as follows:

"The ovarian mass is somewhat rounded and slightly nodular, with an irregular outer surface. It is 7 by 6 by 4.5 cm. The outer surface was a dull gray, and there is evidence of old fibrous adhesions. These adhesions bound the tube down to the surface of the ovary without closing the ampullar end. The cut surface of the ovary is made up of irregular, thick, trabeculae of fibrouslike tissue between which there are numerous pockets of thick, grayish and, after fixation, granular purulent matter. There is no evidence of normal appearing ovarian tissue in the mass. The lumen of the tube is small and apparently empty. The fimbriated end is open.

"The appendix is 4.5 cm. long, the lumen of which is slitlike or obliterated throughout.

*Presented at the Fifty-Third Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons at Excelsior Springs, Mo., September 26 to 28, 1940.

"Microscopically there are large pockets of neutrophiles with numerous mycelia of actinomycosis surrounded by dense granulation tissue in the ovary.

"The tube has pockets of pus in the lumen, the mucosal folds are thickened and densely infiltrated with neutrophiles and lymphocytes. No actinomycosis was found in the tube.

"The serosa of the appendix shows moderately fibroblastic proliferation plus lymphocytic infiltration. No actinomycosis could be found on repeated section."

X-ray pictures taken of the chest while the patient was still in the hospital showed no evidence of lung involvement.

The patient was seen three months after discharge from the hospital at which time she had gained ten pounds in weight. There was no evidence of any inflammatory condition whatsoever in the pelvis.

In November, 1939, one year after operation, bimanual examination revealed no evidence of any tumor masses to be felt anywhere in the pelvis. The patient's general condition was very satisfactory except for a vaginal discharge. Vaginal smears were negative for actinomycosis or trichomonas.

The patient again appeared for examination in August of 1940 with the story that in May, 1940, she developed an abscess of the occipital bone and had been referred to Rochester for surgery. A report from Dr. Love of the Mayo Clinic shows that the patient had an infection in the occipital region with evidence of increased intracranial pressure, bilateral choked discs and a diagnosis of a right cerebral lesion was made. There was a sinus in the right parieto-occipital region. Examination of pus showed no "sulfur bodies" but a *Staphylococcus albus.* She was operated upon and found to have an extensive osteomyelitis of the bone in the occipital and parietal regions. No intracerebral involvement was found. Convalescence was uneventful and her eye symptoms have improved. Our examination in September, 1940, showed small areas of granulation in the wound from which no evidence of actinomycosis could be obtained. The eye ground examination revealed no choking of the discs. An x-ray of the chest was negative. The sedimentation rate was 11 mm. per hour. The leucocyte count was 5,800. The examination of the pelvis was entirely negative and her general condition was good. So there is no evidence found of actinomycosis at the present time.

This case of actinomycosis of the ovary, being the first of its kind that I had ever seen, stimulated a review of the hospital records at St. Mary's and St. Luke's Hospitals for all cases of actinomycosis.

At St. Mary's Hospital there were only three cases to be found over a period of the last twenty years. One case followed an appendectomy with a persistent fistula and pulmonary involvement. This patient died. Another case was that of a young man of a similar type, following appendectomy, but no follow-up could be obtained on this man. There was another case involving the glands of the neck; this patient is still living. The review at St. Luke's Hospital from a period of 1923 to date revealed four cases, including the present one. Two cases were an actinomycosis of the glands of the neck; both of these patients, as far as I was able to determine, are still living. One case was actinomycosis of the bowel with a persistent draining fistula after removal of appendix. The patient finally died. The total in Duluth then, from our two leading hospitals, adds up to 3 cases involving glands of the neck, all patients living; 3 cases involving the intestinal tract and all patients are dead; and this case of actinomycosis of the ovaries, patient still living.

In a review of the literature of actinomycosis of the ovary, the theories and conjectures as to why the ovaries should be involved are exceedingly interesting. The number of cases reported in all the foreign and American literature probably does not exceed 100. Kleine, in an exhaustive review of the foreign literature, reports 80 instances in which the female organs were involved. The route of infection has been ascribed to the mouth or the intestines or the vaginal tract. In the ovary

one wonders whether it may come from the intestinal tract or whether it is direct communication from the genital tract. Kleine believes that the ovaries are affected through contact with the intestinal tract, augmented by the susceptibility of the broken tissues in follicular rupture. Actinomycosis of the ovary must be secondary to some port of entry. A primary infection of the ovary is not reasonable. In this case, however, the cecum and the appendix showed no evidence of primary infection, although one writer is firmly convinced that actinomycosis may invade and pass through the cecum without leaving any evidence or scars remaining after the invasion or the passing through the walls of the cecum, and thus it secondarily involves the ovary. There have been only one or two cases of involvement of the uterus primarily. Jaffé thinks that cases of involvement of the female organs are increasing. Involvement of the parametrium need not necessarily mean involvement of the uterus; it may spread to the parametrium via the ovary. He believes that it is usually secondary to infection of the intestines. One author reports a small abscess of the cervix where actinomycosis was found. Another author reports a case of a woman in the poultry business, who had a prolapse of the uterus, in whom actinomycosis of the uterus developed.

It is generally agreed that an actinomycotic infection by the vaginal route is probably a very remote and very rare occurrence. Strangely enough most of the cases reported occurred in the right ovary, which again leads to the opinion that it is an intestinal infection that is the primary source, because the appendix and cecum are the most common sites in the alimentary canal.

Falls is of the opinion that the grasses and grains, as a source of infection, are somewhat remote; the organism does not form spores but fragmentates, and it is not resistant to heat, cold, or dryness.

Joseph and Summerill report a case of actinomycosis of the right ovary in which the tube was involved. It was their contention that it was the result of a vaginal infection following delivery.

Côté and Tudhope report four cases of actinomycosis of the ovary in which they noted the peculiar appearance of the ovary as found in my case. One could not make the diagnosis until the ovary had been sliced and gave the characteristic appearance as described by the pathologist in my case, i.e., "irregular thick trabeculae of fibrous-like tissue between which are numerous pockets of thick grayish granular purulent material."

V. H. Cornell reported a case which was of long standing before coming under the proper observation. He reviewed the literature also and found 71 published cases of actinomycosis, 45 of which were dead, 8 of them improved, and 7 in which the outcome is doubtful and only 11 which are possible cures.

Rossow was firmly convinced that most cases arise from the bowel. Cordua seems to differ from Falls' opinion and he says that actinomycosis is widespread in moist and dry earth and that the spores are easily transported by the winds to the grasses, grains, vegetables, and fruits, and also found in butter and cheese, the feces of man and animals, and even the teeth of healthy persons, and yet the disease is quite rare. He is inclined to think that actinomycosis is nonpathogenic for most people.

One would like to call this case a primary actinomycosis of the ovary, but how could such an incident happen without more definite proof than we have, in spite of the fact that this case showed no involvement of the appendix or cecum or tubes.

METASTASES

Metastases are reported by some writers to be actually blood borne. It may spread to any part of the body, even the bones. Whether my patient had an extension to the occipital region remains to be seen. At any rate sulfur granules were not found and the wound has entirely healed without any further incident. According to the averages found by most authors as far as cures are concerned, usually some metastatic involvement occurs at some time or another. Needless to say, this patient is so located, near my town, that it will be possible to observe her from year to year.

TREATMENT

The treatment seems to vary from surgical treatment to the use of x-ray and iodides. Many authors think that these patients should have deep therapy and many think they should not. X-ray seems to be particularly helpful, according to Vonessin, in the more superficial actinomycotic lesions, especially those in the cervicofacial area, but he also believes that they should have more intensive treatment than most inflammatory lesions. I think treatment depends entirely upon the location.

Many authors think that iodine should be given to saturation over a long period of time, and there are many who are of an opposite opinion.

Surgery seems to enter into the picture in all cases. In this particular case, I think I have been very fortunate in being able to isolate the specimen, to remove it in toto, and no other treatment has been instituted. The patient is living and well two years later without any apparent evidence of recurrence.

SUMMARY

I have presented the case of a young girl with no characteristic symptoms of actinomycosis, who was operated upon. A tumor of the right ovary was found adherent to the right tube, with no involvement of the appendix, cecum, uterus, or parametrium. The tumor was removed in toto. The pathologic diagnosis is actinomycosis with no areas of actinomycosis found in the tube or appendix. It is hard to conceive that this could be a primary actinomycosis of the ovary; surely there must be some primary source of infection. It may be from the mouth, it may be blood borne, it may be through the intestinal tract through the walls without any scars being observable. At any rate, the case is most interesting, and two years later the patient is very well indeed.

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DISCUSSION

DR. FREDERICK H. FALLS, Chicago, Ill.—This subject is of special interest to this society because of the rarity of the lesion; because of the infrequency with which the correct diagnosis is made clinically, and because of its high mor-

tality rate. Cornell found 71 cases up to 1934; of these, 45 died and only 11, or 15 per cent, were probably cured.

I wish to emphasize that the lesion is found on the right side practically always first, and that it may and often does extend to the opposite side after the removal of the primary lesion. The left ovary and tube are usually not involved at the time of the first operation. The question naturally arises as to the value of a prophylactic panhysterectomy under these circumstances. My opinion is that if there is extensive involvement of the ovary on one side, the fundus of the uterus and the opposite tube and ovary should be removed. The obvious difficulty is the uncertainty of the diagnosis from the gross appearance of the ovary.

It is practically impossible to diagnose the condition clinically until abscess with sinus formation and cultivation of the organism on blood agar slants reveals the typical growth. It is important to note that bacteriologically the growth first is noticed in seven to nine days. This is dry and scaly, and grows with a raised dirty grayish brown border. At operation an inflammatory lesion involving the right ovary or tube and ovary, without evidence of a similar process at work on the opposite side, should make the gynecologist very suspicious that the case is one of actinomycosis. From what I have seen and read of the disease, I should be inclined to do a supracervical panhysterectomy and to avoid spilling any of the pus if possible. I also would feel inclined to place these patients on full doses of potassium iodide and follow the operation with therapeutic x-ray treatments.

I am inclined to classify Dr. Coventry's case as one of primary actinomycosis of the ovary for the reasons he has given and also for the reason that, if some other site of infection had been present, it would probably not have lain dormant during the months and years since operation.

Dr. Coventry is to be congratulated on the outcome of his case to date. It must be remembered, however, that this is a treacherous disease and it is not yet too late for such a misfortune to occur in his case, although highly improbable. I was highly gratified with the immediate postoperative results of the first case of this kind that I observed. But when the lesion recurred on the opposite side and when x-ray and potassium iodide failed to arrest the growth, I became less optimistic.

My second experience with this disease was in May of this year. The woman was 43 years of age, had had the left tube and ovary removed five years previously for ectopic pregnancy. She developed right lower quadrant pain a year and a half before and had metrorrhagia for three months. On examination a rectal fistula was found on the left side of the anus. At operation the uterus was seen to contain a small fibroid, and there was a tumor mass in the region of the right ovary. A supracervical hysterectomy with removal of the ovarian tumor was done.

The ovary measured 4 by 5 by 4 cm. and contained two cystic spaces. The ovary was moderately firm, and on section there were areas of yellow tan tissue. Microscopic sections of the ovary showed an enormous round cell granulation tissue reaction in which well-defined "sun-rayed" and clubbed fungi of actinomyces were found.

Following operation, she developed a pelvic abscess which drained into the bladder and which closed spontaneously. Two weeks later she returned to the hospital with an infected abdominal wound. We were unable to cultivate the actinomyces from the pus from this abscess. Two other abdominal sinuses formed later; she gradually lost weight and strength, in spite of x-ray and potassium iodide in full doses. Sulfanilamide was tried without result and she died June 5, 1940.

DR. LEWIS F. SMEAD, TOLEDO, OHIO.—In 1933 I saw a woman, aged 30 years, with an abscess in her right side. She had been the secretary of a nationally known medical man who had done a lot of experimental work on actinomycosis and had later died of the disease.

In May, 1932, she had been operated upon for what was supposed to be acute appendicitis. In March, 1933, I found her with an abscess under her operative scar which I opened and drained. This was followed by a fistula which refused to heal. She later developed a chronic pelvic inflammatory disease and finally came to operation in July, 1933. Both adnexa were involved, and a supracervical hys-

terectomy was done with the removal of both ovaries and both tubes. The endometrium, the mucosa of both tubes and both ovaries showed a definite infection with the ray fungus.

The incision from this operation healed very well and the pelvic condition has not recurred to date. However, the fistulous tracts in the abdominal wall continued to extend, involving both sides of the abdominal wall from the pubic spine on each side to well above the anterior superior spines and into both flanks. The fistulous tracts were opened and drained many times, and she was given a number of x-ray treatments and huge doses of potassium iodide over a period of four years. There was considerable improvement from the above treatments, but the fistulas persisted. As everything except very radical surgery had failed, it was decided to dissect out these huge sinuses, some of them ten inches long and involving the muscles and other tissues down to the peritoneum. This was followed by large doses of potassium iodide, and by September, 1938, all sinuses were healed, and she has remained quite well to the present time.

DR. COVENTRY (closing).—So far as reinfection is concerned, this may spring up anywhere. It is interesting to find in the literature how frequently it occurs in bones. It does occur, of course, also in the lungs.

The case of Dr. Smead's is the usual story of a patient not coming early and sinuses forming. In any postoperative patient where there is a persistent sinus, the first thing to think of is not foreign bodies but an actinomycosis.

THE TREATMENT OF PELVIC ENDOMETRIOSIS*

WALTER T. DANNREUTHER, M.D., NEW YORK, N. Y.
(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)

EVERYONE doing a large number of pelvic operations must have been impressed by the apparently increasing incidence of endometriosis found in recent years. If Sampson's theory of retrograde tubal cellular spill is applicable in the majority of instances, it seems logical to suggest that the pernicious custom of plugging the vaginal lumen with cotton and other fibrous material during menstruation by the modern woman may be a causative factor. Long before the elegant and much advertised manufactured products were marketed, some women had improvised absorbent cotton occlusions to enable them to dispense with vulvar pads. The different theories of Von Recklinghausen, Cullen, Sampson, Meyer, Robinson, and other authoritative students of endometriosis, regarding its etiology, are well known and require no further elaboration. Although endometriosis is no longer a clinical enigma, its complex nature is not yet fully understood, and the susceptibility of certain women to this disease remains a mystery. Suffice it to say that while the majority of cases are probably due to reversed menstrual flow, a few others may originate as rests of coelomic epithelium, by perforation of hemorrhagic ovarian cysts, by direct implantation, and possibly by lymphogenous or hematogenous dissemination. The term endometriosis is used to include adenomyosis and adenomyoma of the uterus; extrauterine endometrial implants anywhere in the pelvis; involvement of the rectovaginal septum; chocolate cysts of the ovary; endometriosis of bladder, appendix, and colon; endometrioma; and abdominal wall implants following previous laparotomy, particularly after Gilliam's suspension operation and cesarean section. All of these varieties are characterized by the same physiologic response to the hormonal influence of the ovaries as the uterine endometrium. Dougal and others have suggested that by grouping all cases under the headings "internal endometriosis," when the lesions are confined within the visceral peritoneum of the uterus, and "external endometriosis," whenever the glands are found elsewhere, the other designations used for the protean manifestations of what is essentially a uniform pathologic process can be discarded. Unfortunately such a simple classification provides for no distinction between circumscribed tumefactions and a diffuse heterotopia, nor for their locations. Hence, I believe that it is desirable to retain those terms which possibly convey a definite conception of each individual case.

During the past ten years prior to July, 1940, I have operated upon 115 women suffering from endometriosis. Since the treatment of such cases constitutes a surgical problem and the technical details depend

*Read, by invitation, at a meeting of the Boston Obstetrical Society, November 19, 1940.

largely upon the judgment of the individual operator, it seemed best to base this presentation on a limited personal experience rather than to include a much larger series of patients operated upon by others as well as myself. There were 39 instances of adenomyosis; 10 of adenomyoma; 63 of "chocolate" ovarian cyst and widespread endometriosis, and 3 of endometrioma (Table I).

TABLE I. PERSONAL PATIENTS WITH ENDOMETRIOSIS OPERATED UPON WITHIN TEN YEARS

Adenomyosis of uterus	39
Adenomyoma of uterus	10
"Chocolate" ovarian cyst and widespread endometriosis	63
Endometrioma	3
	115

I have seen a number of additional patients in whom a tentative diagnosis of endometriosis seemed warranted, but whose annoyances were not intolerable. The use of progesterone has apparently helped to keep some of these young women comfortable. Another group of women presented clinical evidence of the disease during operation, but since the pathologic reports on the excised tissue failed to verify the diagnosis, all such cases have been excluded from this presentation.

SYMPTOMATOLOGY

The chief symptoms in all forms of endometriosis seem to be abnormal bleeding, pelvic pain, and acquired dysmenorrhea. (Table II).

TABLE II. SYMPTOMS OF ENDOMETRIOSIS IN 115 PATIENTS

71 patients, or 61 per cent, had pain
71 patients, or 61 per cent, had abnormal bleeding
18 patients, or 15 per cent, had dysmenorrhea

Pain, or a sensation of pelvic pressure, may be generalized throughout the pelvis or elsewhere; in the suprapubic region, one of the lower abdominal quadrants, or the sacral area. Dyspareunia is a common complaint, particularly when the structures behind the posterior vaginal fornix are involved. When the rectovaginal septum is indurated by endometriosis, increasing constipation, painful defecation, or a consciousness of rectal pressure may also be noticed by the patient. In some instances the pain radiates down one or both thighs. Abnormal bleeding initiated by endometriosis is characterized by menorrhagia, shortened intermenstrual intervals, or clots. A few patients had a little dirty brown uterine discharge between their menstrual periods, but no one mentioned bright red intermenstrual bleeding.

Dysmenorrhea may be premenstrual, intramenstrual, or postmenstrual. It is sometimes accompanied by vomiting and fainting, and is invariably of recent origin rather than primary.

Other symptoms observed in occasional cases are urinary frequency, leucorrhea, and evident abdominal tumor. Concomitant fibromyoma occurred in a large number of cases, 46 times in 115 cases, or 40 per cent.

ADENOMYOSIS

Adenomyosis implies a diffuse penetration of the myometrium by typical and benign endometrial glands. In reviewing these 39 cases of adenomyosis, without other endometrial lesions, the patients' ages are noteworthy. Only 2 were less than 35, one being 31 and the other 34. The rest ranged from 35 to 56 years, so that ovarian conservation was seldom a serious problem. Every one was subjected to hysterectomy; 34 supravaginal, 4 total, and 1 vaginal in a patient with an incidental procidentia. One or both ovaries were retained in a few patients in whom the diagnosis was not established until the laboratory report was received. One patient had been unsuccessfully treated with roentgen ray therapy for the control of menorrhagia, and another was operated upon three years after a laparotomy for tubal gestation. The diagnosis

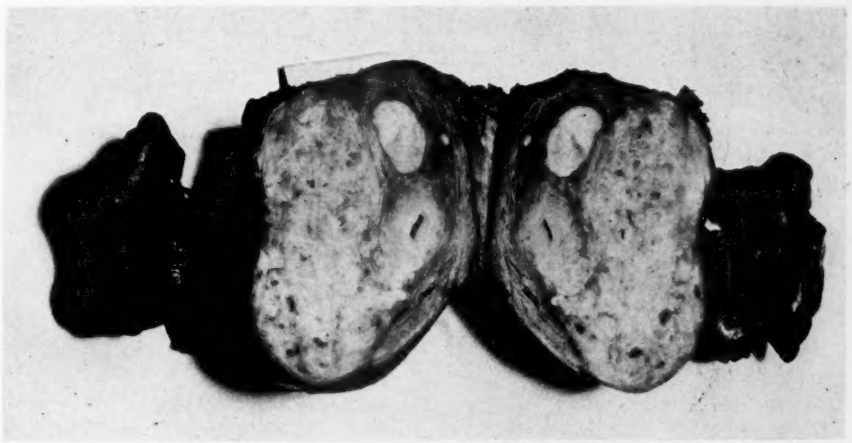

Fig. 1.—Typical adenomyoma of the uterus.

of adenomyosis can be made positively only after uterine extirpation, and it is quite possible that many additional cases are unknowingly and successfully treated with intrauterine radium therapy. In this group of 39 patients treated surgically, the end results were satisfactory.

ADENOMYOMA OF UTERUS

The term adenomyoma of the uterus is applied to a circumscribed nodular area or tumefaction of the myometrium consisting chiefly of endometrial glands (Fig. 1). Grossly it simulates a fibromyoma and, when encountered without evidence of endometriosis elsewhere in the pelvis, may be easily mistaken for an ordinary fibroid. I made this error in 6 of the 10 cases in the series, although 4 of them also showed areas of adenomyosis scattered through the uterine corpus, and 5 of them were accompanied by true fibroids. All but one patient was more than 36 and less than 40 years of age. The exception was a young woman of 28 with a huge symmetrical tumor of the uterine corpus, which produced

severe menorrhagia and pelvic pain. In an effort to be justly conservative I split the myometrium and enucleated the tumor with some difficulty, assuming that I was doing a myomectomy and preserving menstruation and the childbearing function. Only after the specimen reached the laboratory was it evident that I had eviscerated the uterus,

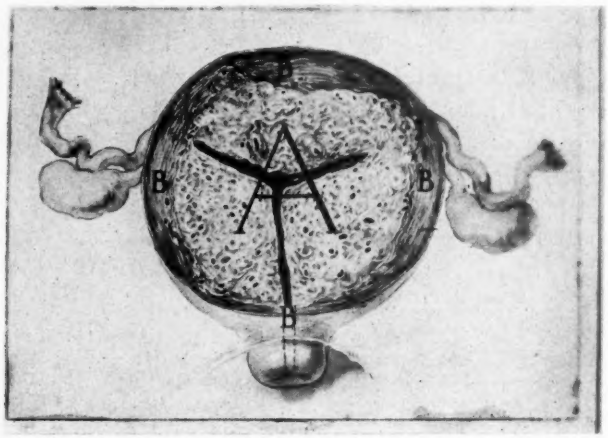

Fig. 2.—Huge symmetrical adenomyoma in a 28-year-old patient, simulating a fibromyoma. *A*, adenomyoma; *B*, shell of myometrium.

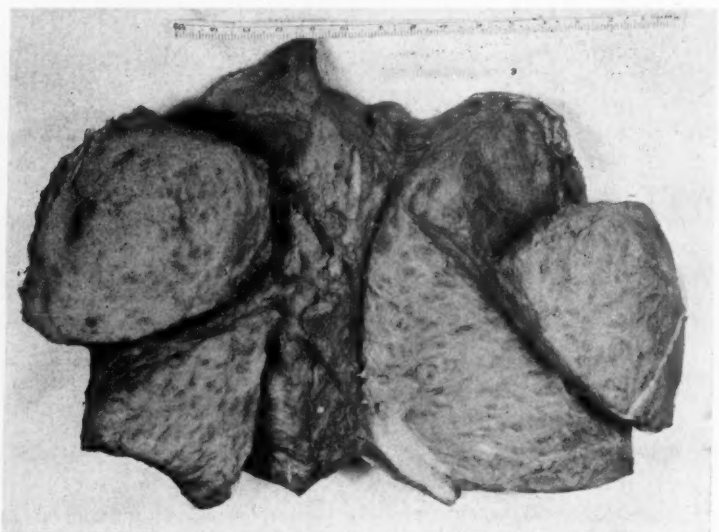

Fig. 3.—Large adenomyoma, previously treated unsuccessfully by another gynecologist with 1500 mg. hours of radium therapy for the control of profuse bleeding.

and that the tumor was an adenomyoma (Fig. 2). Despite the retention of both normal ovaries, this patient has, of course, never menstruated since the operation, as the entire endometrial cavity was included in the extirpated tumor. In two of these cases the adenomyoma encroached upon the bladder to such an extent that hysterectomy was difficult, and

one of them subsequently developed a urinary fistula, which required a second laparotomy for closure. Another patient with a large adenomyoma (Fig. 3) had been previously treated unsuccessfully by another gynecologist with 1,500 mg. hours of radium therapy for the control of profuse bleeding. Coincidentally, chocolate ovarian cysts and involvement of the rectovaginal septum were found in three cases. In general, it can be said that the majority of cases of adenomyosis and adenomyoma of the uterus are found in women of more than 35 years of age; that some form of hysterectomy is necessary for cure; and that conservation of ovarian function is usually a matter of little importance. When unpleasant menopausal symptoms appear, replacement organotherapy affords prompt relief. A follow-up of my 49 patients indicates a satisfactory end result when so treated.

CHOCOLATE OVARIAN CYSTS AND WIDESPREAD ENDOMETRIOSIS

The surgical treatment of widespread pelvic endometriosis is a challenge to the judgment of every operator, principally because 40 per cent of cases occur in women of less than 35 years of age (Table III).

TABLE III. AGE INCIDENCE IN WIDESPREAD PELVIC ENDOMETRIOSIS

	NUMBER OF PATIENTS	APPROXIMATE PER CENT
25-35 years	25	40
36-60 years	38	60

Many gynecologists favor routine radical procedures, including the removal of all ovarian tissue, thus cutting off completely the stream of estrin supply, and thereby insuring prompt regression of implants and protection against reoperation for subsequent extension of the disease. My own practice has been to perform either a supravaginal or total hysterectomy in patients more than 35 years of age, but to conserve as much normal tissue as possible in younger women, and I have so far had no reason to regret it. I believe that it is better to risk the necessity of another operation, than to castrate young women indiscriminately for any benign condition.

In the 63 cases under consideration there were chocolate cysts of the ovary in 56 patients, scattered implants in 24, involvement of the rectovaginal septum in 17, and associated adenomyosis in 9 (Table IV).

TABLE IV. INVOLVEMENTS IN 63 CASES OF WIDESPREAD PELVIC ENDOMETRIOSIS

		APPROXIMATE PER CENT
Chocolate ovarian cysts	56	90
Scattered implants	24	38
Rectovaginal septum	17	27
Associated myometrial adenomyosis	9	15

Chocolate cysts of the ovary were found in women from 25 to 60 years of age. Two patients with large cysts had been subjected to supravaginal hysterectomy with bilateral ovarian retention by other operators,

and two others had been unsuccessfully treated elsewhere with roentgen ray therapy for menorrhagia. It would, therefore, seem that whereas intrauterine radium therapy may be effective in the treatment of adenomyosis, the value of x-ray treatment in some cases of both adenomyoma and cholocate ovarian cysts is questionable.

One patient, 55 years old, operated upon four years previously and still living, had a large papillary adenocarcinoma within a huge chocolate cyst (Fig. 4). Another patient had bilateral multilocular chocolate cysts, in the largest of which there was a benign papillary cyst adenoma (Fig. 5). Chocolate cysts are due to endometrial implants involving the ovary with ensuing hemorrhage, and must be differentiated from corpus luteum hemorrhagic cysts. They can be distinguished

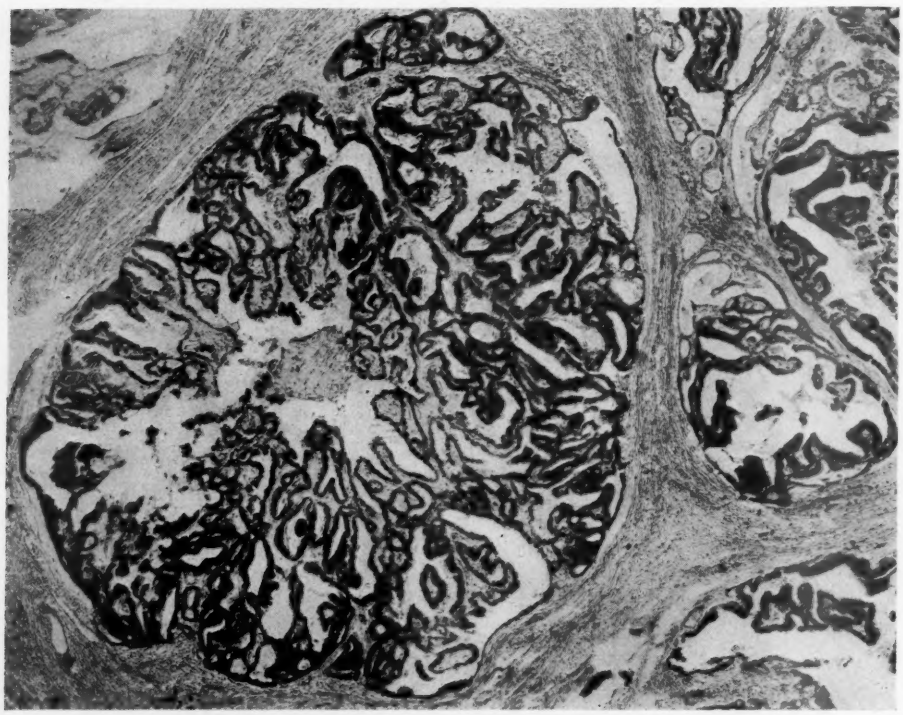

Fig. 4.—Papillary cyst adenocarcinoma formed in the wall of a large chocolate cyst. The papillae are covered with several layers of columnar epithelium. (Multiple chocolate cysts were present.)

from the latter by the evidence of intracystic repeated hemorrhages, irritation in the adjacent structures, and one or two points of rigidity in the cyst wall, which represent the site of the implant. One had a picturesque involvement of the vaginal fornix with blue dome cysts (Fig. 6). Four showed endometriosis of the appendix, and in one of these, aberrant endometrial glands were found in the muscularis, as well as on the visceral peritoneum (Fig. 7). Extension beyond the uterovesical peritoneal fold and into the bladder musculature occurred in two cases, distorting the uterovesical peritoneal reflection in much the same manner as in the two cases in which an adenomyoma infiltrated the bladder wall. Hysterectomy without bladder damage may be extremely difficult under such circumstances, but vesical resection is unnecessary, as the mucosa escapes involvement and ovarian ablation will be followed by rapid retrogression of the lesion. Implants were discovered in the Fallopian tubes in five other cases. In another woman there were extensive im-

Fig. 5.—Benign papillary cyst adenoma in wall of chocolate cyst, 18 by 18 by 6 cm. The columnar epithelium imitates endometrial glands and the stroma resembles endometrial stroma.

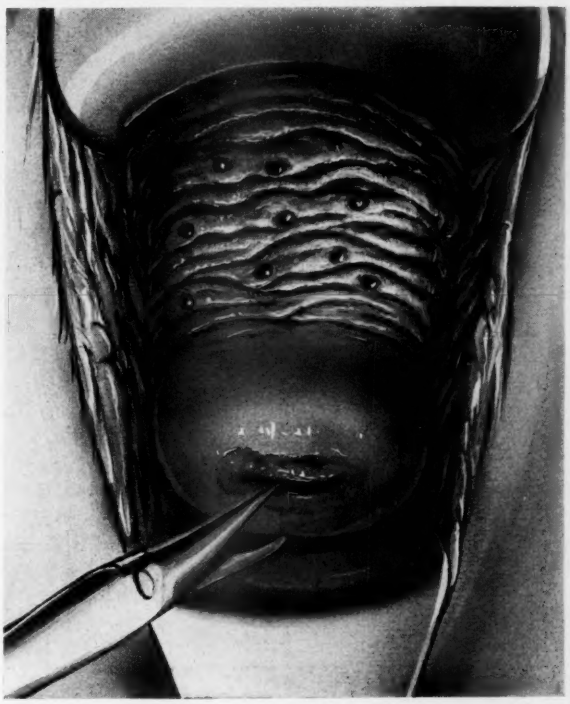

Fig. 6.—Blue dome cysts of the posterior vaginal fornix, filled with chocolate material.

plants in the wall of the colon, a condition which makes complete ovarian removal imperative to prevent subsequent obstruction and to re-establish the gut lumen. It is of paramount importance to differentiate endometriosis from an annular carcinoma of the bowel without palpable metastases, to avoid a superfluous intestinal resection.

Fig. 7.—Endometriosis of the appendix. *A*, points to an endometrial cyst in the musculature, filled with blood. *B*, points to a similar cyst in adhesions between the appendix and oviduct.

In the group of 38 women more than 35 years of age, I removed all ovarian tissue in 32 cases and conserved one or part of an ovary in 6. Supravaginal or total hysterectomy was done in all of these, except the two women whose uteri had been removed previously by another operator. On the other hand, in a group of younger patients, those of 35 years or less, every effort was made to preserve some ovarian tissue (Table V).

TABLE V. OPERATIVE PROCEDURES FOR CHOCOLATE OVARIAN CYSTS AND ENDOMETRIOSIS IN PATIENTS LESS THAN 35 YEARS OF AGE

Unilateral oophorectomy	7
Removal of one ovary and resection of the other	7
Myomectomy and unilateral oophorectomy	4
Hysterectomy and unilateral oophorectomy	2
Hysterectomy and bilateral oophorectomy	5
	25

In 5 instances the involvement of the pelvic structures was so extensive that ablation of the uterus and both adnexa was imperative. More radical surgery is justifiable when the cul-de-sac is densely indurated, but small implants can be destroyed with a fine wire cautery tip. All patients have been conscientiously followed up, but to supplement the records a letter was sent to each of the other 20 young women, asking each to state (1) whether or not she has been well since her operation, (2) whether she has been subjected to another operation elsewhere, and (3) if she has been pregnant since her operation. Replies have been received as follows: all are well but 2, who have moderate pelvic pain and dysmenorrhea. None has required a secondary operation, and 2 have delivered at term, one eighteen months, and the other two years after operation. This incidence of 10 per cent pregnancy is not so insignificant as it may seem, since 4 of the patients were unmarried.

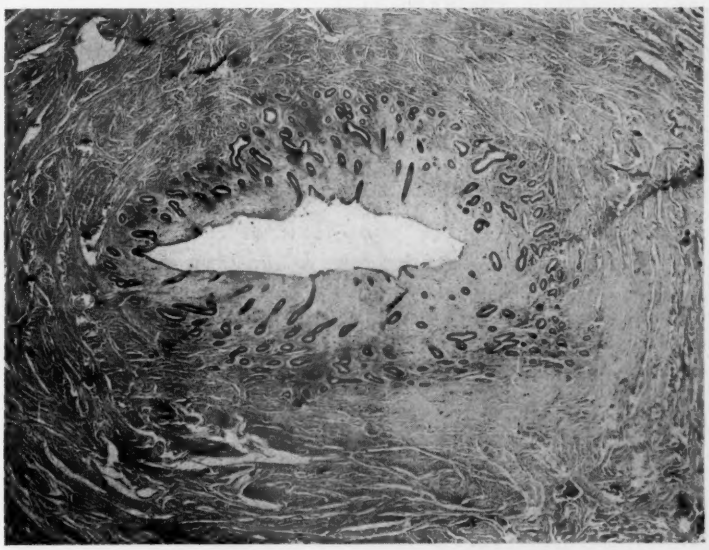

Fig. 8.—Endometrioma of the round ligament. The cyst is lined by endometrium with well-formed glands.

ENDOMETRIOMA

An endometrioma may be defined as a circumscribed tumor, consisting chiefly of endometrial glands extraneous to the uterus, ovaries, and Fallopian tubes. Three such cases were found.

A 23-year-old, unmarried girl was operated upon because of severe menorrhagia, secondary dysmenorrhea, and pain in the right lower abdominal quadrant. In addition to the removal of a large simple serous cyst of the right ovary and the appendix, a nodular mass intrinsic in the right round ligament, about 4 cm. from the uterine cornu, was excised. This tumor, about the size of a hickory nut, proved to be an endometrioma (Fig. 8).

A 34-year-old, unmarried woman presented herself, complaining of severe pain and swelling during each menstrual period, in a tumefaction in the abdominal wall. This patient had been subjected to a modified Gilliam suspension operation of the uterus elsewhere three years previously. A round mobile endometrioma, about the

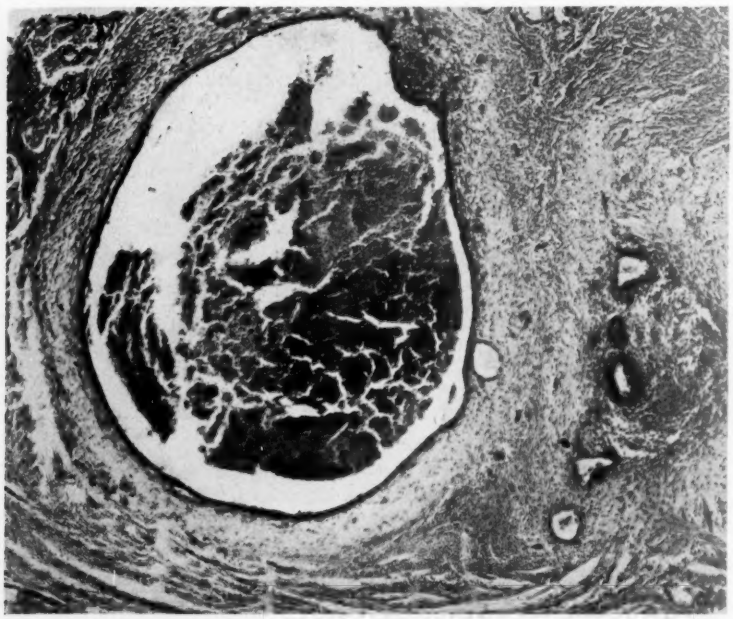

Fig. 9.—Endometrioma of the abdominal wall after a Gilliam suspension. The cysts are lined with endometrial epithelium, the largest being filled with blood.

Fig. 10.—Subserous nodule in the left broad ligament, attached to the uterine cornu, oviduct, and ovary. The tubules are lined with endometrial gland epithelium.

size of a walnut, was located 6 cm. to the left of a lower midline abdominal scar. When excised, it was found in proximity to the site of the round ligament attachment, involving the muscle and fascia (Fig. 9).

A 38-year-old, married woman was subjected to supravaginal hysterectomy and bilateral salpingo-oophorectomy for chocolate cysts and numerous endometrial implants throughout the pelvis. A nodular intraligamentary tumor, simulating a parasitic fibroid in the left broad ligament, proved to be an endometrioma. There were no fibroids in the uterus (Fig. 10).

TECHNICAL DETAILS

It would be presuming for me to suggest the adoption of standardized surgical procedures for the operative treatment of endometriosis. I shall therefore mention only a few technical details which have proved of apparent value in my hands. The most important of these is to defer the actual pelvic operation until the pelvic organs have been freed from all omental and intestinal entanglements, and the normal anatomic relationships have been restored so far as possible. Manipulations designed to mobilize the pelvic viscera should be started by the dissecting hand in the deepest possible recesses of the cul-de-sac and continued upward. Dissecting maneuvers, either sharp or blunt, begun at the top of the agglutinated area result in shredding of tissue, extensive bleeding, and difficulties in general. When a huge tumor mass is impacted in the true pelvis, a longitudinal incision on the anterior aspect of the uterine corpus will facilitate the removal of much of the tumor bulk by either enucleation or morcellation. This permits a lateral collapse of the myometrium, and gives free access to the ovarian and uterine vessels. On the other hand, if the mass is intraligamentary, it can be partly or completely mobilized quite easily by making a parallel incision just below the course of the round ligament and gently detaching the parametrium with the fingers. Chocolate cysts are often extremely thin walled and inadvertently ruptured. The prompt use of suction enables the operator to dispose of the cyst contents immediately and clears the operative field nicely. If the uterovesical fold of peritoneum and the bladder wall are densely infiltrated, it is important to remember that it is wiser to leave some of the uterus attached to the bladder than to jeopardize the bladder wall by overenthusiastic separation. This principle also holds true when the lower uterine segment and rectum are extensively involved. In conservative ovarian procedures in young women, especially after ovarian resection, it has seemed advantageous to shorten the uteroovarian ligament, thus elevating the remaining tissue out of the pelvis and maintaining its position close to the uterine cornu. In some cases there may be remaining areas which cannot be satisfactorily peritonized. Under such circumstances I have utilized one or two sheets of gutta-percha tissue to wall off the intestinal coils and omentum from the pelvis. In the presence of persistent oozing from some raw surface, a gutta-percha cigarette drain with a long iodoform gauze end is of great value. Attempts to clamp and ligate every small bleeding point are futile and a waste of time. All of these drains are brought out of the lower angle of the abdominal wound, removed after forty-eight hours, and have evidently been of service in the prevention of subsequent intestinal obstruction.

CONCLUSIONS

1. The use of progesterone has apparently contributed to the comfort of some young women suffering from endometriosis whose annoyances were not intolerable.

2. Pelvic pain, abdominal bleeding, dysmenorrhea, and dyspareunia are the most common symptoms of endometriosis.

3. Concurrent fibromyomatous tumors were found in 40 per cent of cases.

4. The majority of cases of adenomyosis and adenomyoma are found in women of more than 35 years of age, and hysterectomy is necessary for cure.

5. Forty per cent of cases of chocolate cysts and widespread pelvic endometriosis occur in women of less than 35 years of age, and normal ovarian tissue should be conserved in these young women.

6. Intrauterine radium therapy may be effective in the treatment of adenomyosis, but the value of roentgen ray therapy in cases of adenomyoma and chocolate cysts is questionable.

7. Vesical resection is unnecessary and dangerous in the treatment of bladder wall infiltration.

8. Complete ovarian extirpation is essential for the cure of bladder and intestinal wall involvements.

9. Certain technical operative details which have been described will simplify the operative procedures.

DISCUSSION

GEORGE VAN S. SMITH, BROOKLINE, MASS.—At the Free Hospital for Women we have also had a low operative mortality, 4 deaths among 734 patients with endometriosis treated to date, 0.54 per cent, despite the fact that so often the disease makes operation technically difficult. I wonder whether the low mortality may not be partly accountable to increased peritoneal resistance resulting from more or less constant irritation by the process.

Headache associated with menstruation, sometimes severe, migraine-like and incapacitating, is a symptom I would emphasize as often characteristic of the disease. A history of such cyclic headaches is useful in the differential diagnosis. Furthermore, I have gained the impression that patients with endometriosis are generally highstrung, more than usually nervous and under high internal tension. This impression receives support from their social history, namely, 10 per cent of the married patients in our series were separated or divorced. Parenthetically, 40 per cent were childless. I would tend to blame the disease for the tense state of their nervous systems, for, after all, they have true vicarious menstruation, they have an increased menstruating area without an outlet and so take more menstrual punishment, as it were.

I question the rationale of administering progesterone to these women, beyond the fact that Dr. Dannreuther found it helpful for some with a presumptive diagnosis of endometriosis. Although I have had no experience with hormone trials in this disease, it would be interesting to employ testosterone with the aim of producing temporary inactivity of the ovary and hence endometrium-bearing areas. But would the regression of the ectopic endometrium be permanent? Certainly the hormone would not affect the adhesions and scarring resulting from the disease and to which so much of the symptomatology is attributable. Conceivably the giving of testosterone might be a diagnostic and possibly a therapeutic test and might be of value for postponing operation in a younger patient or as a preoperative measure to put the internal genitalia at rest. I would not want to lean upon hormone therapy more than temporarily in the treatment of endometriosis, both because

of its own pathology and because of its associated pathology. Thus, 50 per cent of our series had fibroids, 7 patients had cancers outside the pelvis, 4 of which were in the breast, 7 had cancer of the cervix, 7 had cancer of the endometrium, and 50 had associated ovarian tumors, of which 15 were malignant, a 5 per cent incidence of ovarian cancer in those with endometriosis over the age of 40. In one instance endometrioma, benign papillary cystadenoma and cancer were found in the same chocolate cyst. Furthermore, in reviewing the microscopic sections of 401 of our series treated before 1935, I found 18 instances in which papillary change was clearly evident in the stroma, indicating that the chocolate cyst was changing into a papillary cystadenoma, a tumor which has marked propensity toward further change into malignancy.

DR. F. A. PEMBERTON.—Regarding etiology we are inclined to feel that transformation of the surface epithelium of the ovary and of the peritoneum play a larger part in chocolate cysts and pelvic sites than is generally supposed and that there may be an endocrine factor also. The disease seems to be more common in single women and in married women who have practiced contraception. Sixty-five per cent have a functional-like menorrhagia and more than half have headache at menstruation. Furthermore, fibroids are a common coincidental finding. Counsellor says that if there is a marked cystic hyperplasia of the endometrium in the uterus the endometriosis will be too extensive for conservative treatment and that, as would be expected, the endometrium in both sites shows the same picture.

Thirteen per cent of our patients showed no tumors in the ovaries, a finding which is well known, but I think it is not generally appreciated that it may happen so often.

The number of different locations of the disease is extraordinary. Its appearance in the cervix and vagina is easily understood, but why is it found so rarely, considering the great number of patients who have a dilatation and curettage followed by plastic operations on the vagina? We have seen only one instance of a perineal tumor following such operations. It may be that endometrium during menstruation has some quality which favors implantation, having been primed with the ovarian hormones perhaps and, since plastic operations are rarely done at that time, endometriosis does not follow.

We are struck by the backache which those patients having the tumor in the uterosacral ligaments complain of. It is fairly constant and much worse during menstruation, and may be present when examination reveals only tenderness in the ligaments with no palpable tumor. It has helped me in making a diagnosis.

We treated 470 patients, proved by pathologic examination, at the Free Hospital for Women up to 1936. We did conservative operations on 30 per cent of them.

If the patients want children, as they often do, we make every effort to save the uterus and some ovarian tissue, being careful to destroy all the implants, that cannot be easily removed, with the fulgurating needle. The patients are followed, and if recurrences appear and careful consideration makes us feel that another conservative operation is not indicated, we use x-ray treatment. We have been struck by the early recurrence in five cases, that is, within two to five months. It seemed as if the operation spread and stimulated the growth.

One reason for doing conservative operations is to conserve fertility. Eighty-three were married and under 40, and 19 (22 per cent) became pregnant, but only 2 of them more than once. It seems to us therefore that, everything else being equal, if a patient has had several children, conservation of fertility is not important since she is likely to have only one more child.

We have been surprised by the low mortality. There was only 1 death, that from pulmonary embolism, in the 470 cases, 329 of which had a supravaginal or complete hysterectomy, and 141 a conservative operation of some type. They were operated upon by the various members of the staff. When one considers the dense adhesions so often dealt with and the trauma to the pelvic wall in the region of the iliac veins, one would expect more thrombotic complications. Perhaps it is a sign of gentleness in handling and of cutting rather than tearing adhesions whenever possible. This low mortality seems to indicate that chocolate cysts are not infected very often.

We have done presacral neurectomies in 10 of the conservatively treated patients but cannot draw any worth-while conclusions as yet. Counsellor has done it in 13 instances and feels that it prevents pain with recurrences, but since the nerve supplies only the uterus and bladder, it would seem that it cannot play a large part in the symptomatology. The neurectomy is done as the first step and the peritoneum closed before separating the pelvic adhesions to avoid retroperitoneal implantation.

Pyogenic infection of a chocolate cyst is a serious complication, for it does not tend to resolve, acting like the ovarian abscesses found in ordinary pelvic inflammation. The adhesions are so dense that one cannot do any extensive surgery without great danger of damaging intestine and spreading infection. It is a rare complication fortunately. My procedure is to drain the abscess and use x-ray treatment after the inflammation has quieted down. In the last one I did the patient still had symptoms from her adhesions, and the hysterectomy done ten months after the original infection proved to be surprisingly easy.

If a patient has had both ovaries removed for endometriosis, should one use estrogen if her climacteric symptoms are bad? It might stimulate renewed growth of the tumor and the patient should be examined frequently. So far I have seen only one questionable bad effect. A woman of 45 had a hysterectomy and bilateral salpingo-oophorectomy done for chocolate cysts. I saw her again two years later complaining of abdominal pain and showing nodules in the posterior cul-de-sac by vaginal examination. A gastrointestinal x-ray was negative. She refused operation, x-ray treatment had little effect, she developed masses throughout the abdomen and died in a few months. No autopsy was allowed. A review of the specimen removed at operation showed no cancer.

She had been treated most of the time for a year with estrogen, but I could not find out how much was used. This is a very inconclusive story, I realize, but it suggests that the estrogen may have stimulated some implants to growth and that cancer developed in them. I think one should be cautious in the use of estrogen for climacteric symptoms after operations for endometriosis.

580 Park Avenue

THE EFFECT OF COMBINED ADMINISTRATION OF CHORIONIC GONADOTROPIN AND THE PITUITARY SYNERGIST ON THE HUMAN OVARY*

Preliminary Report

Charles Mazer, M.D., and Elkin Ravetz, M.D., Philadelphia, Pa.

IT IS now definitely established that the three phases of the ovarian cycle, follicular maturation, ovulation, and luteinization, are evoked by the successive and harmonious action of the two anterior pituitary sex hormones, known as the follicle-stimulating and the luteinizing fractions.

The individual and combined effects of the two pituitary sex hormones are better discernible in hypophysectomized than in normal infantile animals, because even the immature hypophysis of most species contributes to the response of the ovaries to treatment with the gonadotropins. Thus, injections of the follicle-stimulating fraction in rats, five to fifteen days after pituitary ablation, evoke growth of the ovarian follicles but no luteinization. Whereas, injections of the luteinizing principle in hypophysectomized rats causes neither follicular growth nor

*Read in abbreviated form at a meeting of the Texas Association of Obstetricians and Gynecologists, October 5, 1940, and as here presented at a meeting of the Philadelphia Obstetrical Society, November 7, 1940.

luteinization of the granulosa cells. When, however, the two fractions are administered either in succession, first the follicle-stimulating and then the luteinizing fraction, or concurrently, the ovaries of hypophysectomized rats undergo follicular ripening, ovulation, and luteinization.

THE PHARMACOLOGIC ACTION OF THE COMMERCIALLY AVAILABLE GONADOTROPINS

A gonadotropin is an ovarian and testicular stimulant, regardless of its source. The available gonadotropins are derived from animal pituitaries, pregnant mare serum and human pregnancy urine.

Animal pituitaries yield mostly the follicle-stimulating hormone, very little of the luteinizing principle. The separation of the two hormones is not only difficult but also impractical, because both elements are needed to produce a complete ovarian cycle. Pituitary gonadotropic extracts, if given in sufficient quantity, evoke follicular growth, ovulation, and luteinization in the ovaries of intact immature and hypophysectomized animals alike. They are, however, insufficiently concentrated for therapeutic use.

The blood of pregnant mares yields a considerable quantity of gonadotropin which is effective in both the intact and hypophysectomized test animal. It is, therefore, believed to be identical with the sex hormones of the anterior hypophysis.[1] The equine gonadotropin is, moreover, sufficiently concentrated to produce multiple ovulation in some women.[2, 3] Clinically, equine gonadotropin seems to be most effective in the treatment of sterility due to anovular menstruation. In its present concentration, it is, however, almost useless in the treatment of the more common menstrual disorders, amenorrhea and dysfunctional uterine bleeding.

Human pregnancy urine yields a luteinizing principle derived from the placenta. It is, therefore, known as chorionic gonadotropin. In the ovaries of most intact species, it produces all of the effects of pituitary and equine gonadotropins. It is, however, incapable of stimulating to any appreciable degree the ovarian follicles of hypophysectomized animals, intact monkeys, and human beings.[4, 5] It is, therefore, assumed that the pituitaries of animals other than the monkey and the human being contribute, in some unknown manner, to the ovarian response to chorionic gonadotropin.

The undoubted therapeutic value of chorionic gonadotropin in many instances of dysfunctional uterine bleeding must, for the present, be attributed to a mechanism independent of the ovaries.

EARLIER EXPERIMENTS WITH COMBINED CHORIONIC AND PITUITARY EXTRACTS

The observation of Leonard[6] in 1931, that a combination of chorionic gonadotropin and a pituitary extract rich in the follicle-stimulating principle produces in intact immature rats ovarian weights averaging 142 per cent greater than the sum of the increased weights produced by each component individually, was accepted as evidence of the physiologic expression of the combined action of the two gonadotropic principles. Evans and his co-workers[7, 8] observed, however, that the combination of chorionic gonadotropin and hypophyseal extracts relatively free from

gonadotropic hormone also stimulates development of immature rat ovaries (gauged by weight and microscopic appearance) to a far greater degree than could be expected by any additive effect resulting from the use of the two constituents individually. They, therefore, suggested that the element responsible for this effect is present in the hypophysis of the immature rodent as an inactive prohormone which is converted into an active substance by the addition of chorionic gonadotropin.

The observation of Evans that pituitary extracts almost totally free from the follicle-stimulating hormone enhance the activity of chorionic gonadotropin was corroborated by Mazer and Katz[9] in 1933. The latter, moreover, obtained no greater ovarian weight by combining chorionic gonadotropin with a pituitary extract relatively rich in the follicle-stimulating hormone. The results were the same, provided the two dissimilar pituitary extracts represented an equal quantity of pituitary tissue. This observation suggested that it is not chiefly the follicle-stimulating principle which enhances the activity of chorionic gonadotropin but rather an unknown substance in the pituitary extract.

Recently, we obtained from the Research Laboratory of Parke, Davis & Co. freshly prepared extracts of human pregnancy urine (chorionic gonadotropin) and of anterior pituitary lobe tissue, both of which we employed individually and in combination in groups of infantile rats, weighing 30 to 40 Gm. The ovaries of such rats normally have an average weight of from 10 to 12 mg. As seen in Table I, a total of 0.3 mg. of the chorionic gonadotropin preparation, or of 1 mg. of the pituitary extract, employed individually, increased the weight of the ovaries of each of the two groups of test animals to an average of 24 mg., only double that of the controls. However, when the same quantities of the two extracts were given in combination to a group of infantile rats, the average weight of the ovaries increased to 99.4 mg., eight times that of the control animals. Furthermore, it required 8 mg. of the chorionic gonadotropin preparation or 10 mg. of the pituitary extract to produce a 500 per cent increase in the ovarian weight of the immature rats; but the combination of only 0.1 mg. of the chorionic gonadotropin preparation and 0.3 mg. of the pituitary extract produced such a 500 per cent increase. These results cannot reasonably be attributed to a physiologic expression of the combination of the follicle-stimulating and luteinizing principles.

TABLE I. EFFECT OF CHORIONIC GONADOTROPIN AND THE PITUITARY SYNERGIST EMPLOYED INDIVIDUALLY AND IN COMBINATION UPON IMMATURE RATS*

CHORIONIC GONADOTROPIN		PITUITARY SYNERGIST		COMBINATION		
TOTAL DOSE	WEIGHT OF OVARIES	TOTAL DOSE	WEIGHT OF OVARIES	TOTAL DOSE OF CHORIONIC GONADOTROPIN	TOTAL DOSE OF PITUITARY SYNERGIST	WEIGHT OF OVARIES
0.15 mg.	22.4 mg.	1 mg.	23.0 mg.	0.075 mg.	0.25 mg.	50.3 mg.
0.3 mg.	24.3 mg.	2 mg.	42.6 mg.	0.1 mg.	0.3 mg.	58.6 mg.
0.6 mg.	29.0 mg.	4 mg.	47.7 mg.	0.15 mg.	0.5 mg.	70.4 mg.
1.0 mg.	28.3 mg.	6 mg.	43.2 mg.	0.3 mg.	1.0 mg.	99.4 mg.
5.0 mg.	39.5 mg.	8 mg.	48.1 mg.			
6.0 mg.	49.5 mg.	10 mg.	55.2 mg.			
8.0 mg.	63.2 mg.					
10.0 mg.	72.5 mg.					

*Average weight of control infantile rat ovaries, 10 mg.
Each determination represents the average ovarian weight of each of 5 infantile rats

Knowing that even nonspecific substances, such as egg albumen and zinc sulfate, can convert the follicle-stimulating hormone into a luteinizing principle,[10] it is reasonable, in the light of the facts cited above, to suspect that there is some unknown element in the pituitary component of the extracts employed which renders chorionic gonadotropin so much more potent.

EXPERIMENTS ON THE HUMAN BEING POINTING TO THE EXISTENCE OF A PITUITARY SYNERGIST

The most important indication that the anterior hypophysis probably produces a substance which converts the species-selective chorionic gonadotropin into a universal gonadotropin is the phenomenal response of the human ovary to a combination of chorionic gonadotropin and a pituitary extract containing very little of gonadotropic activity, because neither of the two administered individually exerts the slightest influence on the human ovary. Chorionic gonadotropin, regardless of its concentration, does not stimulate the human ovary; the available pituitary gonadotropins are insufficiently concentrated for use in the human female. Nevertheless, the combined administration of the two seemingly inert extracts produces a degree of stimulation of the human ovary far in excess of the normal requirement.

The product we employed in 23 patients preoperatively is, as stated above, a combination of chorionic gonadotropin and a pituitary extract containing very little of gonadotropic substance (Table I). It is commercially known as synapoidin. One cubic centimeter of synapoidin yields 15 synergy units. A synergy unit is the minimum quantity which, when given in 6 divided doses over a period of three days, increases the weight of the ovaries of infantile rats 500 per cent. The pituitary component in the synergy unit of synapoidin is only one-thirty-fifth of the quantity which, when employed alone, is capable of evoking a similar increase in weight of the ovaries of infantile rats. The chorionic gonadotropin component of the synergy unit of synapoidin is only a seventy-fifth of the quantity that gives a similar ovarian response in infantile rats.

Twenty-three patients, varying in age from 12 to 46 years, were each given 75 to 315 synergy units over a period of from one to eighteen days before laparotomy for various gynecologic conditions. Twenty of the twenty-three patients showed macroscopic evidence of stimulation in the form of oversized ovaries, multiple hemorrhagic follicles, and, in many instances, multiple incompletely-formed corpora lutea. Only one of the 16 patients in whom one or both ovaries were removed at operation failed to show microscopic evidence of intense stimulation.

The degree of the ovarian response seems to depend upon the receptivity of the ovaries, the total dosage and the duration of treatment. Thus, the ovaries of three regularly menstruating, young women in this group were overstimulated to a pathologic degree. In each, the ovaries were 8 to 10 cm. in diameter and studded with numerous hemorrhagic follicles which ruptured and bled at the slightest touch. The uteri were enlarged, soft and congested, simulating early pregnancy. However, in premenopausal women, the ovarian response apparently varies inversely with the degree of pre-existing sclerosis. In some, one

TABLE II. GROSS AND MICROSCOPIC APPEARANCE OF THE OVARIES OF 23 WOMEN WHO RECEIVED PREOPERATIVELY INJECTIONS OF A COMBINATION OF CHORIONIC GONADOTROPIN AND THE PITUITARY SYNERGIST

RECORD NO.	AGE	TOTAL NUMBER OF SYNERGY UNITS	DURATION OF PREOPERATIVE TREATMENT	TIME RELATION OF EXPECTED FLOW TO LAPAROTOMY	GROSS APPEARANCE OF OVARIES		MICROSCOPIC APPEARANCE OF OVARIES		TYPE OF ENDOMETRIUM
					RIGHT	LEFT	RIGHT	LEFT	
A18983	45	150	5 days	15 days	Small and sclerotic	2 large hemorrhagic follicles	Sclerosis	2 early corpora lutea	Secretory
A19238	32	150	5 days	10 days	1 corpus luteum	3 clear follicles	1 corpus luteum	Not excised	Secretory
A19876	35	315	14 days	1 day	Moderately enlarged; 2 corpora lutea and 3 hemorrhagic follicles	Serous cyst	Not excised	Serous cyst	–
A19552	42	315	7 days	7 days	3 hemorrhagic follicles	2 hemorrhagic follicles	1 corpus luteum and 2 hemorrhagic follicles	2 hemorrhagic follicles	Secretory
A20035	43	180	6 days	11 days	Large serous cyst; 1 large hemorrhagic follicle	3 hemorrhagic follicles	Serous cyst; 1 early corpus luteum	2 hemorrhagic corpora lutea; 1 hemorrhagic follicle	Secretory
A20207	46	180	6 days	18 days	Sclerotic	Enlarged; 1 corpus luteum and 4 hemorrhagic follicles	Old corpus luteum	Fresh corpus luteum; 4 hemorrhagic follicles	Proliferative
A20450	28	270	12 days	1 day	Both ovaries the size of tangerines; distended with many hemorrhagic follicles		4 corpora lutea in various stages of development	Not excised	Secretory
A20443	31	210	7 days	7 days	Both ovaries the size of average lemons; studded with many hemorrhagic follicles		1 corpus luteum; many hemorrhagic follicles beginning luteinization	Not excised	Secretory
A20511	35	90	2 days	16 days	1 corpus luteum	Dermoid cyst; 3 hemorrhagic follicles	Not excised	Dermoid cyst; 2 small corpora lutea, 2 hemorrhagic follicles	–
A20948	43	60	One injection	Metrorrhagia	Sclerotic; 1 hemorrhagic follicle	3 hemorrhage follicles	Not excised	Not excised	–
A21022	12	60	One injection	23 days	No hemorrhagic follicles		Not excised	Not excised	–

A21514	42	180	7 days	14 days	Enlarged; 1 corpus luteum and 4 hemorrhagic follicles	Enlarged; 3 hemorrhagic follicles	1 fresh corpus luteum; 3 hemorrhagic follicles	3 hemorrhagic follicles one undergoing luteinization	Late proliferative
A21519	41	210	10 days	5 days	Both ovaries the size of lemons; distended with many hemorrhagic follicles		2 corpora lutea; 2 hemorrhagic follicles	Not excised	Secretory
A21520	43	120	4 days	Amenorrhea	3 hemorrhagic follicles	1 corpus luteum; 2 hemorrhagic follicles	3 hemorrhagic follicles, 1 beginning luteinization	1 corpus luteum; 2 hemorrhagic follicles	Secretory
A21567	32	120	8 days	7 days	1 corpus luteum; 4 hemorrhagic follicles	1 corpus luteum; 3 hemorrhagic follicles	Not excised	Not excised	–
A20559	33	180	4 days	Amenorrhea	4 hemorrhagic follicles	1 corpus luteum; 4 hemorrhagic follicles	Many hemorrhagic follicles, some showing beginning luteinization	Not excised	–
A21986	41	180	12 days	Amenorrhea	Small and sclerotic	Small and sclerotic	Sclerosis	Not excised	Proliferative
A22053	34	150	7 days	1 day	Enlarged; 4 hemorrhagic follicles	1 corpus luteum and 1 hemorrhagic follicle	Not excised	1 corpus luteum and 1 hemorrhagic follicle	Secretory
A22275	44	195	6 days	Metrorrhagia	Enlarged; 3 hemorrhagic follicles	Size of lemon; 2 large hemorrhagic follicles	2 corpora lutea and 1 hemorrhagic follicle	1 corpus luteum and 1 hemorrhagic follicle	Secretory
A22380	45	240	10 days	1 day	1 large and 1 small corpus luteum	1 small corpus luteum	2 fresh corpora lutea	1 old corpus luteum	Secretory
A22447	14	120	5 days	1 day	Enlarged; 1 large corpus luteum, and 1 hemorrhagic follicle	Enlarged; 1 large hemorrhagic follicle	Not excised	Not excised	–
A22557	24	240	12 days	3 days	Both ovaries size of oranges, deep blue in color, oozing blood from many points		Not excised	Not excised	–
A23188	42	165	5 days	8 days	2 corpora lutea; 4 hemorrhagic follicles	Dermoid cyst	1 corpus luteum; 4 hemorrhagic follicles, 2 with beginning luteinization	Dermoid cyst	Secretory

ovary was definitely stimulated, though not much enlarged, while the corresponding ovary remained small and highly sclerotic. In a girl, 12 years old, a single injection of 125 synergy units three days before operation for subacute appendicitis evoked no changes that could be discerned by mere inspection. In another girl of the same age, the preoperative administration of double the quantity, spread over a period of five days, caused a considerable increase in the size of the ovaries and the appearance of several hemorrhagic follicles (Table II).

Careful microscopic study of the removed ovaries of 16 patients revealed multiple hemorrhagic follicles with luteinized granulosa layers in all but one. Multiple small and large aberrant corpora lutea, hemorrhage into the stroma, and intense edema were present in the ovaries of some of the younger patients. In other words, in young normally functioning women, the larger doses caused a profound disruption of the whole follicular apparatus. The microscopic appearance of the overstimulated ovaries approximated that observed by Hartman[11] in monkeys which received large doses of equine gonadotropin with or without the chorionic luteinizing principle.

Concerning possible deleterious effects resulting from such treatment, Hartman states: "It is, therefore, a justifiable conclusion that the manifestly deleterious action of the extracts employed is temporary, and that recovery is prompt and complete. No facts have come to light which would lead one to condemn the use of gonadotropic extracts in attempts to help sterile women when they are desperately desirous of having children."

In 11 of 14 patients in whom hysterectomy or curettage of the uterus was performed simultaneously, the endometrium showed a pronounced secretory phase; in two, the endometrium was only proliferative in type though the ovaries contained fresh corpora lutea; in the remaining 1 of the 11 women in this group, the endometrium was atrophic and the ovaries sclerotic despite adequate preoperative treatment. This does not imply that the secretory endometrium in the 11 patients was the result of treatment, for only one of them was frankly amenorrheic.

For obvious reasons, the preoperative treatment with synapoidin was short in most of the 23 patients. In planning the use of the product for therapeutic purposes, one should seek to imitate the normal length of the human menstrual cycle and administer the product in smaller doses for twenty days of the month.

CLINICAL EVALUATION OF SYNAPOIDIN THERAPY

Therapeutically, we have thus far employed synapoidin in only 49 carefully selected patients. Those treated for mild forms of menstrual disorders are not included in this report. Twenty-three of the patients had varying degrees of persistent amenorrhea; 18 were suffering from severe menorrhagia or metrorrhagia; and 8 were sterile mainly because of failure of ovulation.

Effect on Amenorrhea.—Of the 23 amenorrheic patients, 3 had never menstruated and 11 had not menstruated for one or more years. Only 9 of the group had one to three periods during the year preceding treatment with synapoidin. All of them had previously been treated by other means, without relief.

Amenorrheic patients received 5 to 10 injections of 30 synergy units of synapoidin every other day. Second or third courses were given soon after the cessation of an induced menstrual flow or, in the event of failure, about two weeks after the last injection.

Regardless of the duration of the amenorrhea, only 4 of 23 women failed to menstruate after one or two courses of injections. In fact, one of the patients, aged 20, who had never menstruated, had her first menstrual flow five days after the last

TABLE III. AVAILABLE DATA ON THE TREATMENT OF TWENTY-THREE SEVERELY AMENORRHEIC WOMEN

PATIENT	AGE	NO. OF MENSTRUAL PERIODS DURING YEAR PRECEDING TREATMENT	TYPE OF AMENORRHEA	SIZE OF DOSE	NO. OF INJECTIONS PER MONTH	NO. OF MONTHS TREATED	NO. OF INDUCED MENSTRUAL FLOWS	COMMENT
B. C.	24	0	Secondary	30 u.	15	1	0	Treatment in progress
R. D.	29	0	Secondary	30 u.	8	2	2	Treatment in progress
A. E.	24	0	Secondary	15 u.	10	2	2	Treatment in progress
H. F.	25	0	Secondary	30 u.	9	2	2	Treatment in progress
E. G.	19	3	Secondary	30 u.	6	3	2	No spontaneous periods
L. H.	23	3	Secondary	30 u.	7	3	2	No spontaneous periods
F. H.	19	0	Secondary	30 u.	10	2	2	Treatment in progress
N. L.	20	1	Secondary	30 u.	5	5	5	Treatment in progress
G. V.	27	0	Secondary	30 u.	5	1	1	No follow up
E. C.	36	1	Secondary	30 u.	8	2	1	Treatment in progress
G. M.	27	0	Secondary	30 u.	10	2	2	Treatment in progress
G. G.	27	3	Secondary	30 u.	8	2	2	Treatment in progress
F. B.	27	0	Secondary	30 u.	7	3	1	No spontaneous periods
J. R.	17	2	Secondary	30 u.	10	2	1	No spontaneous periods
A. R.	30	3	Secondary	30 u.	5	2	0	No spontaneous periods
R. S.	28	3	Secondary	30 u.	7	3	3	Treatment in progress
C. S.	28	0	Secondary	45 u.	6	2	2	4 spontaneous periods
H. W.	28	0	Secondary	45 u.	5	2	2	No spontaneous periods
R. D.	20	0	Primary	30 u.	10	2	1	Treatment in progress
L. K.	30	2	Secondary	15 u.	10	2	2	2 spontaneous periods
A. B.	22	0	Secondary	30 u.	5	3	3	Treatment in progress
A. D.	24	0	Primary	30 u.	10	1	0	
R. J.	30	0	Primary	30 u.	15	1	0	Treatment in progress

of 10 injections of 30 synergy units each. Excluding the four patients who proved totally resistant to this form of therapy, 45 courses of injections in the remaining 19 patients thus far evoked menstrual bleeding 38 times (Table III). An 84 per cent response to single courses of injections is very encouraging, *since it implies renewed ovarian activity and not merely withdrawal bleeding as in estrogen replacement therapy.* We must, nevertheless, remember that these results are far from conclusive, since only 2 of the 23 amenorrheic women have thus far menstruated without treatment. The majority of them are still under treatment.

From our limited experience in the treatment of severe cases of amenorrhea, it appears that injections of this product should be given in gradually reduced doses thrice weekly for twenty days of each month for a period of six consecutive months. The individual dose of the first and second courses of treatment should, in our opinion, be no less than 30 synergy units. From a more extensive experience in the treatment of the milder forms of amenorrhea (oligomenorrhea), it appears that half of the above-mentioned dose given similarly over a period of three months is sufficient in most instances.

Effect on Dysfunctional Uterine Bleeding.—The results with one course of from 5 to 20 injections of similar doses in 18 patients suffering from dysfunctional menorhagia or metrorrhagia are more striking than in amenorrhea. The patients varied in age from eleven to thirty-nine years and were bleeding abnormally for a considerable length of time. In 14 of the 18 patients, the bleeding was arrested during a follow-up period of from two to six months (Table IV). Four of these 14 were puberal girls in whom uterine bleeding is so often most resistant to all forms of therapy until nature establishes a normal pituitary-ovarian balance.

TABLE IV. RESULTS OF TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING IN EIGHTEEN PUBERAL GIRLS AND WOMEN OF CHILDBEARING AGE

PATIENT	AGE	TYPE OF BLEEDING	MONTHS OF BLEEDING	SIZE OF DOSE	NO. OF DOSES	PRELIMINARY CURETTAGE	RESULT	MONTHS OF FOLLOW-UP PERIOD
M. B.	33	Metrorrhagia	3	30 u.	10	None	Relieved	5
B. B.	14	Metrorrhagia	1	30 u.	10	None	Relieved	4
S. G.	11	Metrorrhagia	1	30 u.	10	None	Relieved	2
N. H.	19	Menorrhagia	10	30 u.	10	None	Not relieved	
M. K.	35	Menorrhagia	10	30 u.	11	None	Relieved	2
H. P.	27	Menorrhagia	6	30 u.	10	None	Not relieved	
H. M.	24	Menorrhagia	24	30 u.	5	None	Relieved	2
G. S.	18	Metrorrhagia	1	30 u.	6	None	Relieved	2
M. L.	14	Menorrhagia	8	45 u.	10	None	Relieved	3
E. L.	27	Metrorrhagia	2	30 u.	6	None	Relieved	2
S. M.	33	Metrorrhagia	1	30 u.	15	None	Relieved	4
L. R.	31	Metrorrhagia	1	30 u.	10	None	Relieved	3
S. M.	31	Metrorrhagia	1	30 u.	5	Hyperplasia	Not relieved	
R. R.	21	Metrorrhagia	2	30 u.	10	Proliferative	Relieved	4
A. S.	27	Metrorrhagia	2	30 u.	5	Atrophic	Relieved	2
C. W.	17	Metrorrhagia	3	30 u.	20	None	Relieved	3
J. Z.	20	Metrorrhagia	4	30 u.	5	None	Relieved	3
M. B.	24	Metrorrhagia	30	15 u.	20	None	Not relieved	

Anovular Menstruation.—Only 2 of 8 women with anovular menstruation as the chief cause of sterility conceived soon after synapoidin treatment. They received 5 injections, each 15 synergy units, during the first half of the menstrual cycle and conceived promptly. Most of the others received larger doses which, in the light of our observations during laparotomy, overstimulate the normal and partly active ovaries to a pathologic degree. This is also suggested by the fact that the larger doses either shortened or lengthened the menstrual interval, depending on the time in the cycle at which treatment was terminated. Thus, if the larger doses were

given during the first half of the cycle, the menstrual flow tended to appear in from five to eight days prematurely. If, on the other hand, total doses larger than 150 synergy units were administered during the second half of the cycle, until the day of the expected flow, there was a delay of from four to five days in the appearance of the menstrual flow.

In these regularly menstruating women, as well as in some of those who were given injections of synapoidin preoperatively, the menstrual rhythm after withdrawal of treatment was not disturbed, suggesting that even overdosage does not produce lasting harmful changes in the ovaries. In fact, the intermittent administration of 900 synergy units of synapoidin in the course of three months to one of our sterile patients, not included in this report, not only corrected the tendency to delay of her periods but also resulted in conception one month after the withdrawal of treatment.

SUMMARY

In the human subject, in whom neither chorionic gonadotropin nor pituitary extracts exerts any appreciable influence on the ovaries (the latter because of lack of concentration), the combination of relatively small quantities of each produced definite stimulation and overstimulation of the ovaries in 20 of 23 patients who received the product preoperatively.

Therapeutically, the combination of chorionic gonadotropin and the anterior pituitary extract evoked one or more menstrual flows in 19 of 23 severely amenorrheic women, some of whom had not menstruated for years, despite all other forms of treatment. Only two have thus far menstruated without further treatment.

Injections of the combined extracts arrested dysfunctional uterine bleeding in 14 of 18 patients, 4 of whom were puberal girls.

Only 2 of 8 women in whom anovular menstruation was presumably the main cause of the barrenness conceived promptly. Overdosage and the presence of other etiologic factors partly explain the lack of responsiveness of this group of patients.

The increased effectiveness of chorionic gonadotropin with the addition of a pituitary extract containing very little of the gonad-stimulating hormones is variously explained as follows:

1. That it represents merely the expression of the combined physiologic activity of the two gonadotropins.

2. That chorionic gonadotropin probably converts a prohormone, supposedly present in the pituitary extract, into an active gonad-stimulating hormone.

3. That most anterior pituitary extracts contain a principle capable of converting chorionic gonadotropin into a universal gonad-stimulating substance.

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DISCUSSION

DR. S. LEON ISRAEL.—The investigations of the past decade have made available three types of gonadotropin: pituitary, chorionic, and equine. It has also become increasingly apparent that, despite these three, the physician is still in need of a gonadotropin suitable for clinical use in selected patients. The pituitary hormone is really not available in satisfactory form. The chorionic derivative is, at best and in some mysterious manner, useful in dysfunctional uterine bleeding, for, so far as the human being is concerned, it is not really a gonadotropin. The equine gonadotropin, while seemingly potent in the human female, is somewhat disappointing in clinical trials and is, moreover, a horse serum that may give rise to atopic reactions and antigonadotropic responses. We now have a preliminary report concerning the biologic potency and possible clinical value of still another type of gonadotropin.

The essayists presented convincing experimental evidence to support the contention that a startlingly effective gonadotropin results from combining minute quantities of a gonadotropic-free pituitary extract with the relatively inert chorionic gonadotropin. It is not necessary to discuss this apparent fact, a fact which the authors' tables establish. We should, however, give some pause to the possible clinical effects of this synergistic combination, the newest of the gonadotropins.

The appearance of even a *single* episode of uterine bleeding in 19 of 23 severely amenorrheic women is an accomplishment of great interest when it is evoked through the mediation of the ovaries. It would naturally be of even greater interest were the future follow-up studies to establish the existence of a normal menstrual rhythm in some of the 19 women. Even if this does not occur, it may be hoped, in view of its ovarian field of action, that further refinement of the synergic combination will yield such a desirable effect. The excellent result attained in 14 of 16 patients with dysfunctional uterine bleeding make one wonder whether or not this salutary effect is simply the result of enhancing the antibleeding power of chorionic gonadotropin, the mechanism of which is unknown. The side-effects noted on the normal menstrual cycle are certainly not in support of that viewpoint, inasmuch as chorionic gonadotropin never disturbs the menstrual rhythm. It is likely that the alteration of the cycle results from an overproduction of estrogen, the effect of which is to inhibit the function of the anterior hypophysis.

It is certainly not fair to attempt to pass judgment on the clinical merit of a potent gonadotropin but recently brought to trial and preliminarily reported to us. It is, however, pertinent to indicate that this presentation raises several important questions which embody the chemical and pharmacologic properties of the pituitary synergist, the proper dosage to employ in order to avoid overstimulation and the therapeutic future of anovular menstruation. From the data presented it appears that the combined gonadotropin is a powerful stimulator of ovulation in the human being. Will it, we may well ask, eventually be shown that this substance gives rise to multiple ovulation of *normal* character, that is, will it result in human superfecundation? Some light may be thrown on this important question by further studies on the endometrium and by assays of the sodium pregnanediol glucuronide excreted by the treated patients, for these represent criteria of ovulation and luteal function. It is also not unreasonable to hope that this synergistic gonadotropin will be subjected to rigorous clinical trials and continued study before its release to the profession at large.

A COMPARATIVE STUDY OF MALE AND FEMALE PELVES IN CHILDREN WITH A CONSIDERATION OF THE ETIOLOGY OF PELVIC CONFORMATION*

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IT HAS been well established by the roentgenologic studies of Thoms,[1, 2] Caldwell and Moloy[3, 4] and others that adult female pelves vary considerably in conformation. These authors[3-6] have shown that the variations in pelvic shape are significant with respect to the mechanism of labor, and that certain types are associated with a high proportion of obstetric difficulties. Recently Thoms and Greulich[7] have shown that adult male pelves also vary considerably in conformation. These studies have brought out clearly that the older definitions of a "normal female pelvis" and of a "normal male pelvis" do not hold in many instances. Thoms'[7] recent study has also revealed that there are no marked differences in the pelvic inlets of men and women, but that irrespective of the particular type, the male pelvis has a smaller capacity than that of the female.

The factors which are responsible for the variations in pelvic shape have yet to be elucidated. It would be of great interest to know whether all human beings start out with pelves of essentially the same shape, which later become molded into one of several characteristic variations, or whether the differences found in adults are present in embryonic life. In 1899 Arthur Thompson[8] published the report of a study of 8 fetal pelves, 4 of which were male and 4 female. Thompson contended that there were characteristic differences in the pelves of the two sexes. It seemed apparent from his study that the characteristics of adult male and female pelves were present in fetal life. His drawings and photographs are quite convincing, yet distortion of the fetal pelvis due to dissection and to fixation is very possible, so that it seems unwise to accept Thompson's views unreservedly, especially in view of the small number of pelves which he studied. The final form of the pelvis may well be influenced by disease, nutrition, general development, and the sex hormones. The latter may even be responsible for the final sex differences observed in adult male and female pelves.

It has not been possible to establish a direct relationship between disease and pelvic conformation except in two notable instances: rickets and osteomalacia. The former produces anteroposterior shortening of the inlet and is probably responsible for the majority of the so-called platypelloid or flat pelves, a small proportion of which has been reported in every series. Osteomalacia is the cause of a marked pelvic deformity

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which fortunately is rarely seen in this country. Tuberculosis and anterior poliomyelitis are occasionally indirectly responsible for asymmetrical pelves, by throwing one limb out of function so that undue pressure is exerted on the good side during formative years when the bones are still soft. Other nutritional and developmental factors may well play important roles in the formation and final shape of the pelvis, but thus far it has been impossible to make such correlations. Sex-endocrine factors are undoubtedly of *great* importance in the development of the ultimate form of the pelvis, although it is not yet settled as to just when these factors exert their influence. Racial differences undoubtedly occur also, but may in part be due to nutritional and other habits typical of different races rather than to a true ethnologic factor.

This study was planned as an attempt to clarify some of these questions. It was decided first to study roentgenologically, by a modification of the Thoms' method, the pelves of children of different ages in order to determine the pelvic shape from early childhood through adolescence and to compare the incidence of the various types with the incidence in adulthood. Although valuable in indicating whether pelvic type is predetermined or develops from a common form into the varieties which are known to exist in adults, there are limitations to the significance of such data. Developmental factors can be studied satisfactorily *only* by studying individuals at different periods of their lives; e.g., yearly from an early age through adolescence. A small beginning has been made upon this phase of the problem, and it is hoped that at some time it may be possible to say definitely whether the pelvis of any one individual starts as a certain type and remains so, or changes with increasing years. This represents a long-time study and will take years to complete.

MATERIAL

The children studied were unselected except as to age and the absence of bony deformity which would interfere with the pelvic roentgenogram. The children were obtained from the pediatric wards, and in a few instances from the outpatient clinic. Most of them were suffering from a variety of conditions, none of which seemed to have a conceivable relationship to skeletal development. In other instances the children were perfectly well. Their ages varied from 4 to 15 years. In children less than 4 years old, ossification has not progressed sufficiently to permit accurate study by the x-rays. A total of 59 girls and 16 boys has been studied to date. The ages given are those attained at the last birthday.

METHOD

Three films were taken in each case to illustrate (1) the superior strait, (2) the lateral aspect of the pelvis, and (3) the subpubic angle.

1. The views of the superior strait were taken as advised by Thoms.[1, 2] The child sits in a semi-reclining position against a back rest. Perpendiculars are then dropped to the table from the lumbar interspace 4 – 5 and the symphysis. The perpendiculars are measured and the points at which they meet the table are marked. After one exposure is made the patient is removed from the table. A Thoms' lead plate with 1 cm. spaced perforations is placed in the plane of the superior strait as indicated by the upper extremities of the perpendiculars mentioned above and a second exposure is made. Great care must be exercised in placing the patient squarely on the table so that a true roentgenogram of the superior strait will be obtained. A perfect picture is one in which the obturator foramina are obscured from view, showing that the superior and inferior pubic rami are directly in line. If the patient

is not squarely placed on the table the pelvic inlet will appear asymmetrical and one obturator foramen will appear more prominent than the other.

A roentgen film taken in this manner affords one the opportunity to measure the diameters of the pelvic inlet as well as to study its configuration.

2. The lateral view of the pelvis is taken with the child standing against the unexposed film, so that the distances between the middle of the symphysis and the film, and between the interspace between the fourth and fifth lumbar spines and the film are equal. Great care should be taken again in lining up the patient so that the trochanters are superimposed one upon the other. A preliminary exposure is made with the patient in this position; the patient is then removed and the Thoms' lead plate placed in the plane of the midpelvis and a second exposure made.

This exposure gives a lateral view of the pelvis with the trochanters superimposed. The centimeter dots are in scale with the midpelvis so that a definite check of the anteroposterior diameter of the inlet can be made by mensuration. It is also possible to study the lateral bore of the pelvis, the width of the greater sciatic notch, the configuration of the sacrum, and the size and shape of the ischial spines.

Because of lack of understanding and lack of cooperation on the part of the younger children studied, it was necessary to take some of the lateral views with the children lying on the table on their sides. Precautions similar to those employed for the standing position were taken to place the lead plate in the midpelvic plane. Maintenance of the correct position on the table was facilitated by placing sandbag supports at suitable points.

3. The subpubic angle was filmed according to the method advised by Pettit and others.[9] The patient lies on her back on the table. The x-ray tube is aimed at the pelvic outlet by tilting it to an angle of 30 degrees. The resultant picture permits measurement of the subpubic angle by a geometric protractor and gives an idea of the splay of the side walls of the pelvis.

RESULTS

It was impossible to obtain perfect pictures in many instances, particularly among the younger children, but the majority of the pictures were satisfactory for the determination of pelvic type. The diagnoses of pelvic types were based upon the definitions set down by Caldwell and Moloy,[3, 4] with special reference to the shape of the pelvic inlet. There were, however, certain variations seen in the pelves of the younger children which will be commented upon later. Caldwell and Moloy have constructed a diagram, of which Fig. 1 is a copy, which illustrates clearly and succinctly the types into which they have divided pelves. While only the characteristic inlets are represented in the diagram, their classification is based upon a consideration of other features also, such as the width of the sacrosciatic notch, the subpubic angle, the splay and bore of the pelvis, etc. These features have likewise been noted in this study. In addition many different diameters have been measured. The points of interest which have come out of these notations will be commented upon in the appropriate places.

The results which were obtained in the 59 girls are given in Table I.

Of the entire number of 59 girls, 42, or 71.2 per cent, had anthropoid pelves, and in 10 others the pelves exhibited anthropoid tendencies although they could not be called pure types. In 6 cases the pelvic inlet was gynecoid in configuration. Three of these 6 children were older girls, 14 and 15 years of age. Of great interest is the fact that in 36 of the 37 girls 11 years old or younger, the pelves were either purely anthropoid in shape or exhibited marked anthropoid tendencies. (See footnote to Table I.)

A similar finding has been recorded by Greulich and Thoms,[10] who as far as we are aware, are the only other observers who have studied the pelves of children by

modern roentgenometric methods. Thoms' classification is somewhat different from that of Caldwell and Moloy so that direct comparison between the two is impossible. He found, however, in his study of 107 young girls, 5 to 15 years of age, that 82.2 per cent had dolichopellic (the anthropoid type of Caldwell and Moloy) pelves. While he studied only 7 children less than 10 years of age, all but one of these had dolichopellic or anthropoid pelves. The older the children, the smaller the proportion of anthropoid pelves became. It would appear from our study and that of Thoms that the pelvic inlet in young girls is characteristically a long narrow oval, the anthropoid pelvis. It is not strange that basically the human female pelvis should approach in shape that of the great apes and primitive peoples. As the child approaches sexual maturity, there seems to be a tendency to anteroposterior flattening,

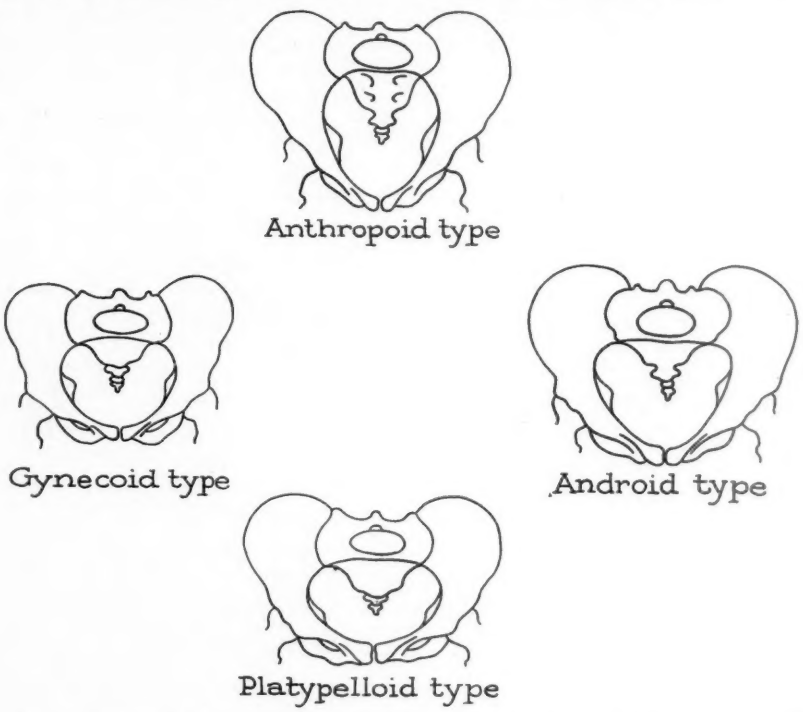

Fig. 1.—Representations of the pelvic inlet in the four main types of pelves. For the sake of simplicity the combination types are omitted. (Adapted from Caldwell and Moloy.)

so that one finds increasing proportions of gynecoid pelves. Whether this tendency is purely the result of sexual maturation or represents the additional influence of extraneous factors such as nutrition, disease, etc., is unknown. This tendency toward anteroposterior flattening is well illustrated by comparing the incidence of the various pelvic types in children and in adult women (Table II).

Thoms[12] made a similar comparison which illustrates the same principle in another terminology (Table III).

While the term anthropoid fits the pelvis of the youngster better than any other, there are several outstanding differences between the adult anthropoid pelvis, as described by Caldwell and Moloy,[3, 4] and that of the child, Fig. 2. The inlet of the adult anthropoid pelvis is an oval, with the long diameter running anteroposteriorly, while that of the child does not present a smooth oval outline. In the latter instance, as the side walls of the inlet sweep forward they bend inward in the regions of the acetabula as if the lateral pelvic walls could not quite withstand the inward thrust of the femoral heads. This feature was seen uniformly in

TABLE I

AGE	ANTHROPOID	GYNECOID-ANTHROPOID	ANTHROPOID-GYNECOID	GYNECOID	ANDROID-ANTHROPOID
5 and less	5	4*			
6	2				
7	4				
8	6				
9	3				
10	3				
11	9			1	
12	5	1		1	
13		2		1	1
14	1		2	1	
15	4		1	2	
Total	42	7	3	6	1
Percentages	71.2	11.8	5.1	10.2	

*These four pelves looked exactly like the five classified as anthropoid in this age group, but are classified here because the transverse diameter of the inlet was slightly greater than the anteroposterior diameter of the inlet.

TABLE II

TYPES OF PELVIS	CHILDREN 5-15 59 CASES (PER CENT)	U. C. SERVICE 410 CASES HAYDEN[11] (PER CENT)	CALDWELL MOLOY[4] 215 CASES (PER CENT)	PETTIT AND OTHERS[9] 100 CASES (PER CENT)
Gynecoid	10.2	54.0	39.5	51
Gynecoid-android		9.0	11.1	
Gynecoid-anthropoid	11.8	6.0	4.6	
Android		2.0	11.6	21
Android-gynecoid		2.0	5.1	
Android-anthropoid		0.7	3.7	
Anthropoid	71.2	16.0	11.6	18
Anthropoid-gynecoid	5.1	2.0	6.5	
Platypelloid		4.2	6.0	5
Asymmetrical		2.0		5

TABLE III

TYPE	104 STUDENT NURSES	582 CLINIC WOMEN	107 CHILDREN
Dolichopellic	73 %	37.3%	82.2%
Mesatipellic	13.5%	27.5%	9.3%
Platypellic	13.5%	35.2%	8.4%

TABLE IV

AGE	ANTHROPOID	GYNECOID-ANTHROPOID	ANDROID-ANTHROPOID
5	1	1	
7	3		
8	1		
9	1		
10	1		
11	1		
12	2		
13	2		
14	2		
15			1
Total	14	1	1

the pelves of the children who were still in their pre-puberty years. On the whole, the posterior half of the child's pelvis has almost a gynecoid configuration, while the anterior half is distinctly anthropoid. This was noted particularly in the younger children, 5 and 6 years of age. In several of these, while the greatest transverse diameter of the inlet actually exceeded the anteroposterior diameter, the general conformation was that described above, and suggested immediately the anthropoid type. However, this group has been classified as gynecoid-anthropoid in order to conform as closely as possible to the classification of Caldwell and Moloy.

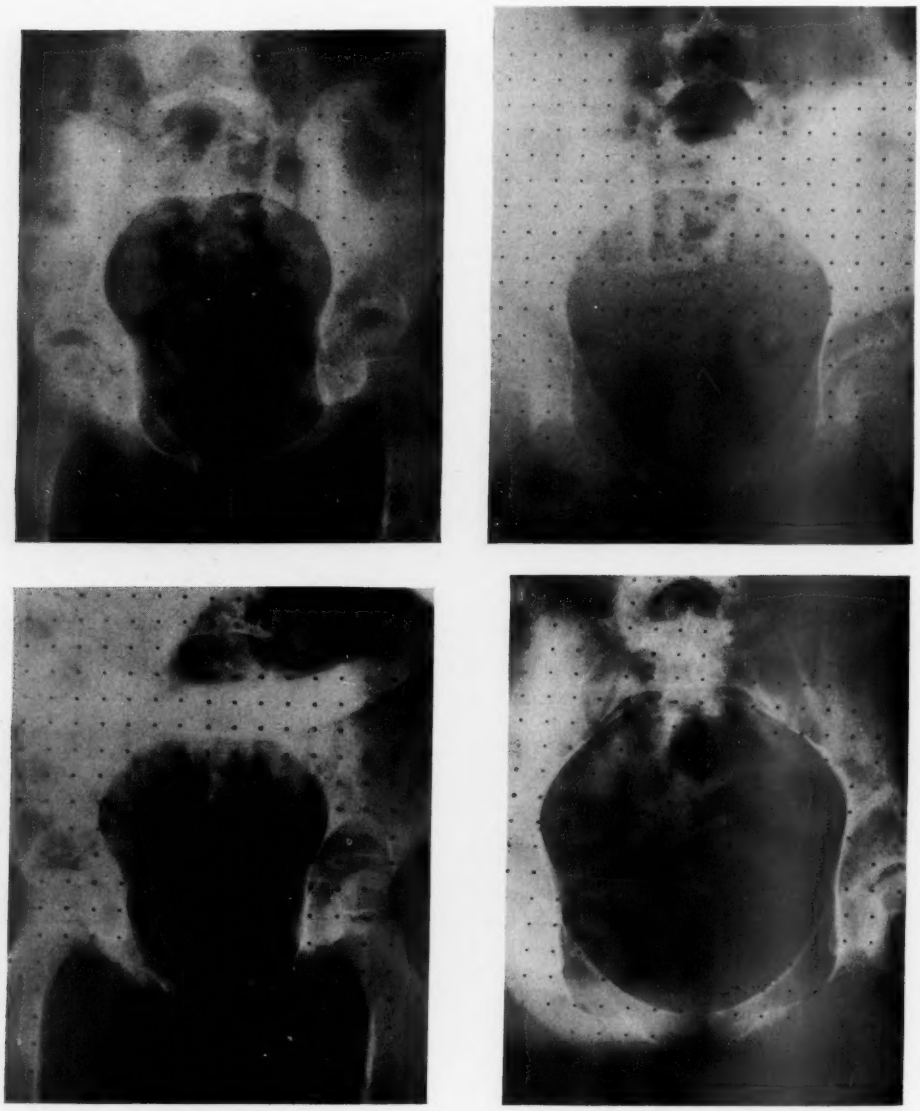

Fig. 2.—The pictures on the left represent examples of the infantile type of anthropoid pelvis. The upper one is from an 11-year-old girl, 4 feet 5 inches tall. The lower one is from a 7-year-old girl, 4 feet 2 inches tall. The inward bowing in the acetabular regions is striking. The pictures on the right represent the adult type of anthropoid pelvis. The upper one is from a 12-year-old girl, 4 feet 10 inches tall, whose pelvic measurements are almost adult. The lower one is from a 15-year-old girl, 5 feet 5 inches tall.

At the present time we are engaged in studying the pelves of pre-adolescent and adolescent boys. To date 16 boys between the ages of 5 and 15 years have been studied. The results are given in Table IV.

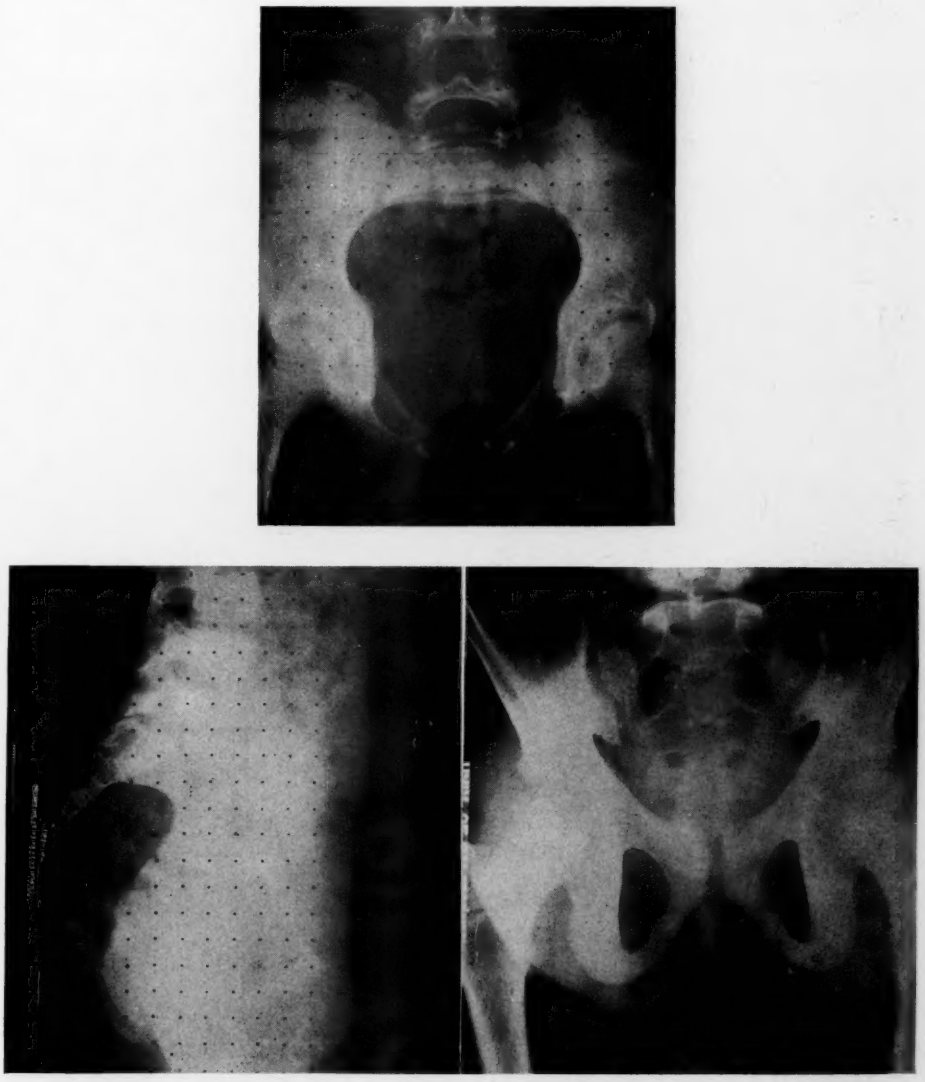

Fig. 3.—A typical case study in a 9-year-old girl, 4 feet 5 inches tall, showing the characteristic oval inlet with the inward bulge in the acetabular regions, the wide sacrosciatic notch, and the relatively high pelvis with rather narrow subpubic angle.

The pelves uniformly were of the anthropoid type similar to that described for the girls, with the exception of one in a boy 15 years old in which distinct android tendencies were seen. Indeed, the pelves of boys who were 11 years old and younger, that is, those boys in the frankly pre-puberty age group, were indistinguishable from those of the pre-pubertal girls. Not only was this true in regard to the shape of the pelvic inlet, but also with respect to the sacrosciatic notch, the subpubic angle and the general appearance of the bones.

In one respect only was a difference observed in the pelves of the two sexes, and as the number of observations is as yet so small one does not know how much importance to attach to this difference. The greatest transverse diameter of the inlet in the young boys was, on the average, closer to the sacrum than was that in the young girls. This fact was revealed by comparing the following quotients

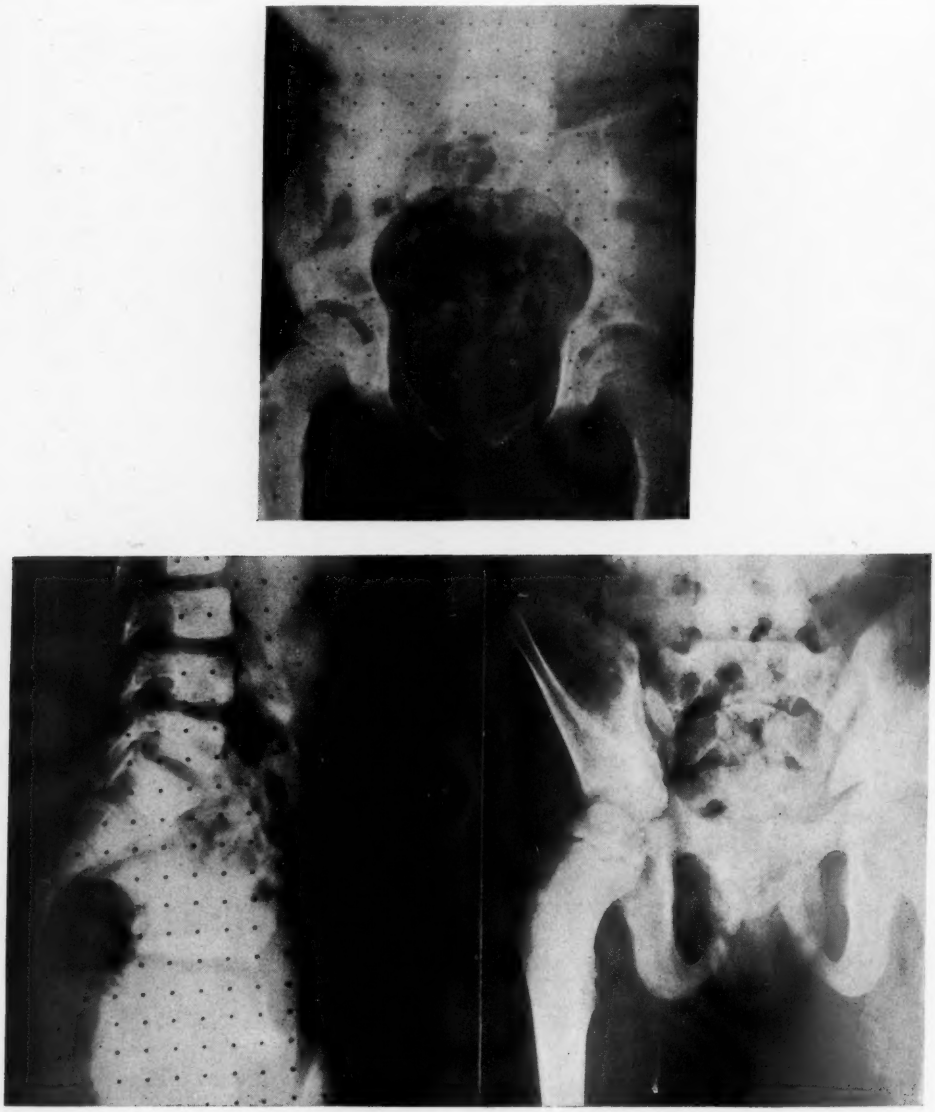

Fig. 4.—A typical case study in a 7-year-old boy. Note the similarity to the findings in the young girls as shown in Figs. 2 and 3.

in the two sexes: AP/AS, where AP represents the anteroposterior measurement of the inlet and AS represents that portion of the AP diameter lying anterior to the greatest transverse diameter of the inlet. Thus, the longer the AS, the smaller the quotient, and the closer the greatest transverse diameter to the sacrum. The average of the quotients in the 16 boys was 1.507; for the boys under 12 years of age, 1.538. The average of the quotients in 25 girls under 12 years of age was

1.610, a considerably larger figure. Thompson observed that such a difference existed between the two sexes in the fetal pelves which he studied. Furthermore, adult male pelves characteristically differ from adult female pelves in having smaller posterior segments at the inlet. Hence, while on the films the pelves of the young boys and girls appear identical, measurement reveals a possible characteristic difference, present early in life, before the changes of puberty.

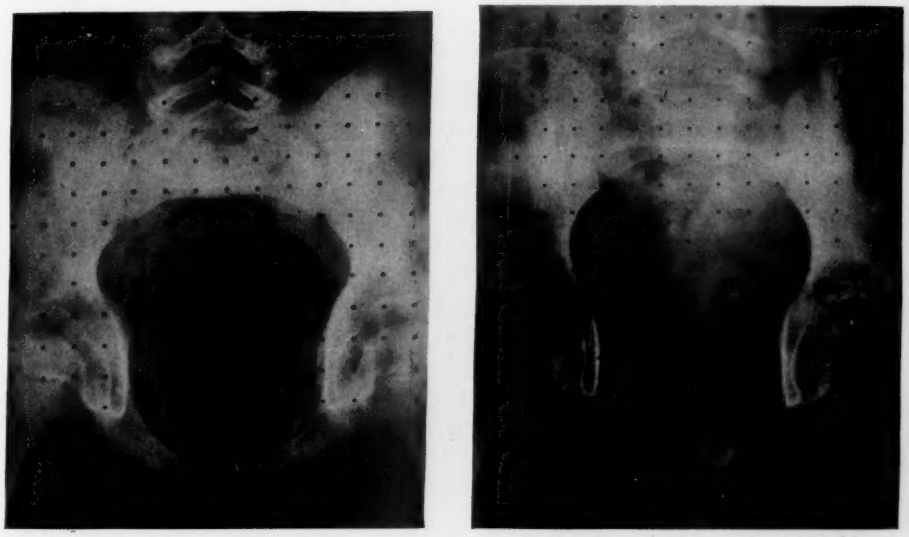

Fig. 5.—Left: Pelvic inlet of a boy 11 years old. Right: Pelvic inlet of a boy 10 years old. Note the marked similarity to the inlet of young girls as illustrated in Figs. 2 and 3.

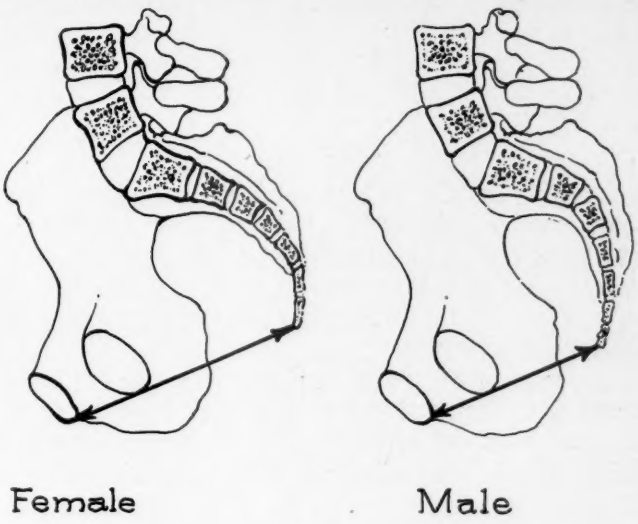

Fig. 6.

DISCUSSION

While the small number of individuals studied does not justify sweeping conclusions, the findings suggest that all human beings, male or female, are born with pelves which are most nearly comparable in their

contours to the anthropoid pelvis of adults; that the greater part of the evolution of the pelvis to its final characteristic male or female form takes place at about the time of puberty and is therefore probably due to sexual factors although there may be inherent differences in the pelves of the two sexes before puberty. Other factors than sex undoubtedly play a role because the final form of the pelvis in adult women and men we know to be quite variable. As to how these factors operate we are still in ignorance.

Although not many of the children studied had matured sexually for more than two or three years, the pelves of the children of post-puberty age exhibited definite changes from those of the younger children, and distinct differences between the two sexes were seen. In the older girls the gynecoid tendency (primarily, an anteroposterior flattening of the inlet) was much more prevalent than in the younger girls. In the older boys the pelvic inlet looked not unlike the anthropoid inlet seen in the older girls. The features which distinguished the older boys' pelves from those of the young boys and from the female pelves were the perceptibly increased heaviness of the bones, the greater height of the pelvis, and the generally narrower subpubic angle. What appeared to be even more characteristic than actual narrowness of this angle was the greater height of the symphysis pubis. This necessitated a backward displacement of the available space at the pelvic outlet. We were unable to observe any particular narrowing of the sacrosciatic notch, a feature which has been designated by many as one of the chief points of differentiation between male and female pelves. We did note, however, that the sacrum of the older boys seemed to angle downward in a way not seen in the female pelves, so that, with the comparative narrowness of the subpubic angle the male pelvis exhibited a definite narrowing and consequent diminution in capacity toward the outlet. This feature is illustrated in Fig. 6.

SUMMARY

The pelves of 59 girls and 16 boys between the ages of 5 and 15 years were studied roentgenologically by a modification of the Thoms' method.

In 42 (71.2 per cent) of the girls and in all of the boys, the pelvic inlet was anthropoid or dolichopellic in type. In 10 other girls, while the pelves were not of the pure anthropoid type, marked anthropoid characteristics were observable.

In all except one of the children of pre-puberty age (11 years or less), both girls and boys, the pelvic inlet was essentially anthropoid in type. Uniformly these inlets exhibited an inward bulge in the regions of the acetabula.

The pelves of the prepubertal children were indistinguishable with respect to sex, except for a possible difference in the position of the greatest transverse diameter of the inlet.

In the children of post-pubertal age, there were definite developments in the pelves which distinguished them from those of the younger children; there were also marked differences between the pelves of the two sexes.

These findings suggest that both males and females start out life with pelves which are identical *in type* and that the major differences observed in adult male and female pelves do not appear until puberty and are therefore due to the influence of the sex hormones.

This study does not suggest a reason for the variations seen in the adult pelves of either sex, but other factors than sex, such as nutrition and disease, probably play major roles.

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SOME OBSERVATIONS ON THE GYNECIC EMPLOYMENT OF EQUINE GONADOTROPINS*

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During the past decade alternate enthusiasm and pessimism have characterized clinical studies of gonadotropic therapy. At present, chorionic gonadotropins** have few champions among gynecologists: consensus of opinion denies their ability to induce ovulation in hypofunctioning ovaries. Pituitary gonadotropins† have not been available commercially in sufficient concentrations to warrant any significant clinical expectations. The clinical availability of equine gonadotropins,‡ a natural result of the important studies of Davis and Koff,[1] aroused considerable clinical interest. The fact that, as Davis and Koff demonstrated, these substances were capable of inducing ovulation in healthy women, i.e., those with receptive ovaries, led to enthusiastic therapeutic expectations and to a number of reports of successful treatment of women with irregularities of bleeding and sterility. Critical objective studies by Huber and Davis[2] and by Gray[3] of the responses of women with spontaneous ovarian failure to therapy with equine gonadotropins have indicated that in some instances apparently normal ovarian responses have resulted. Erving, Sears and Rock,[4] however, in a study

*Read by invitation at a meeting of the Chicago Gynecological Society, October 18, 1940.

**Prepared from pregnancy-urine, commercial preparations include *antuitrin-S, follutein, APL.*

†Prepared from the pituitary glands of animals, commercial preparations include *maturity factor, gynatrin.*

‡Prepared from the serum of pregnant mares, commercial preparations include *antex, gonadogen, gonadin, anteron.*

comprising 48 women with ovarian failure reported that "in no case was there any definite evidence of stimulation of ovulation by equine gonadotropic hormone."

Reports from our clinic[5] were among the first to call attention to the fact that chorionic gonadotropins were not true ovarian stimulators. With this experience as a background, we have been cautious to avoid any uncritical enthusiasm regarding the equine gonadotropins.[6] We have questioned repeatedly the likelihood of the majority of patients with ovarian failure responding to gonadotropic substances, regardless how pharmacologically effective they were, since no proof had been submitted that the genesis of most ovarian failure is due to primary pituitary failure. In instances, wherein ovarian failure results from inadequate pituitary stimuli, the administration of potent and qualitatively ample gonadotropic extracts may permit successful complemental circumvention, at least temporarily, of the pituitary failure.

It has been our belief that before a true and equitable evaluation of gonadotropic therapy is possible, our knowledge of functional pathology and clinical diagnosis must be expanded; we must recognize the etiologic factors, endocrine and nonendocrine, which are involved in the production of ovarian failure, and we must be able to diagnose and segregate the causative factor or factors in the individual patient who requires therapy.

Diagnostic methods at present are not sufficiently practical or conclusive to permit in many instances a clear-cut differential diagnosis as to the pathogenesis of ovarian failure. While it is relatively easy to recognize hypothyroidism as a primary cause of ovarian failure, we cannot gauge the degree or character of the failure of the ovaries by the severity of the metabolic disturbance; at times the failure may be only of gametopathic character, while in other instances it may be fundamentally endocrinal.[7] Microscopic studies of bits of endometria secured by biopsy within the first twelve to eighteen hours after the onset of flowing yield valuable diagnostic data and may permit fairly safe assumptions as to the occurrence or nonoccurrence of ovulation. Minor grades of ovarian failure cannot be recognized by these studies. The end results of ovarian failure reflected in the architecture of the endometrium yield no clues as to the cause of this failure. Data of essentially the same diagnostic import but with, perhaps, more limitations are secured from time-consuming and laborious determination of daily urinary titers of the pregnanediol-complex (one of the metabolic products of progestin). We do not believe that quantitation of this compound permits a numerical expression of the severity of ovarian failure. Our ability to establish the level of pituitary function is extremely limited. Roentgenograms of the sella turcica done routinely supply significant data in only about 2 per cent of the patients. Estimations of gonadotropic titers in the blood and urine have proved notoriously unreliable. One of our greatest needs at present in the diagnosis of the cause of ovarian failure is an accurate and practical method for the quantitation of gonadotropic titers in the blood. This desired diagnostic aid would permit the segregation of hypopituitary ovarian failure

from those of other causes. It would seem inconsistent with rational therapy to give gonadotropins to patients having initially high gonadotropic titers in their body fluids. Such a condition (increased gonadotropic titers of body fluids) is said to occur in association with late ovarian failure of the primary and intrinsic sort and under these circumstances Watson, Smith and Kurzrok[8] have shown that the ovaries are refractive not only to the intrinsic gonadotropins but also to large amounts from extrinsic sources.

The purpose of this communication is the presentation of some observations upon the clinical use of equine gonadotropins in the attempted treatment of ovarian failure. No intention exists of reporting a complete résumé of this experience. An attempt will be made to outline and develop certain general principles related to the clinical uses and limitations of the gonadotropins in gynecic practice.

THE TREATMENT OF ADOLESCENT HYPO-OVARIANISM

Classical adolescent hypo-ovarianism is one of the most clear-cut syndromes in endocrine gynecology. The symptoms, signs, and clinical course of patients with early ovarian failure are too well known to justify detailed description. No or minimal sexual maturation occurs. The internal and external genitalia remain infantile or juvenile in size and character. Adolescent differentiation of the breasts does not occur or progresses to a minimal degree. Menarche does not occur. The skeletal pattern is commonly a characteristic one with the span exceeding the height and the lower measurement exceeding the upper measurement. The epiphyses of the long bones remain open well past the seventeenth or eighteenth year of age and there develops frequently a characteristic statural overgrowth.

It is assumed commonly that the ovarian failure of these patients is intrinsic to the ovaries, i.e., the ovaries are regarded as being structurally incapable of responding to the tropic influences of the pituitary. The fact that these individuals often grow taller than normal women is taken to be evidence that no pituitary failure (certainly of the growth-promoting function) exists. Doubtlessly, these assumptions are true in general, but the fact that significant therapeutic results have been secured in an occasional patient who possessed all the classical symptoms and signs of this syndrome suggests that pituitary failure of the gonatropic functions may coexist with normal pituitary function as regards growth-promoting influences. A therapeutic trial of gonadotropic therapy in this syndrome is necessary, therefore, to establish the need for pituitary therapy, i.e., the presence or absence of pituitary failure (gonadotropic).

The following case is reported as an instance in which there occurred a successful response to equine gonadotropic therapy:

CASE 1.—G. R., colored, single, aged 17 years, was seen first in the Endocrine Division Oct. 13, 1937, because of delayed menarche, statural overgrowth, and sexual underdevelopment (Fig. 1). Gynecologic and endocrine surveys yielded the following data: The breasts were hypoplastic. The axillary and pubic hair were scanty. External genitalia were of juvenile type. The uterus and cervix were

juvenile; entire length of the uterus and cervix was 1 inch; the cervix measured approximately ¾ inch. Ovaries could not be felt. The vaginal epithelium was of immature type. Span exceeded height and lower measurement exceeded upper measurement. Basal metabolic rate was –4 per cent. Roentgenogram of the sella turcica was normal. Epiphyses of the long bones were open and the osseous age was estimated to be 14 to 15 years.

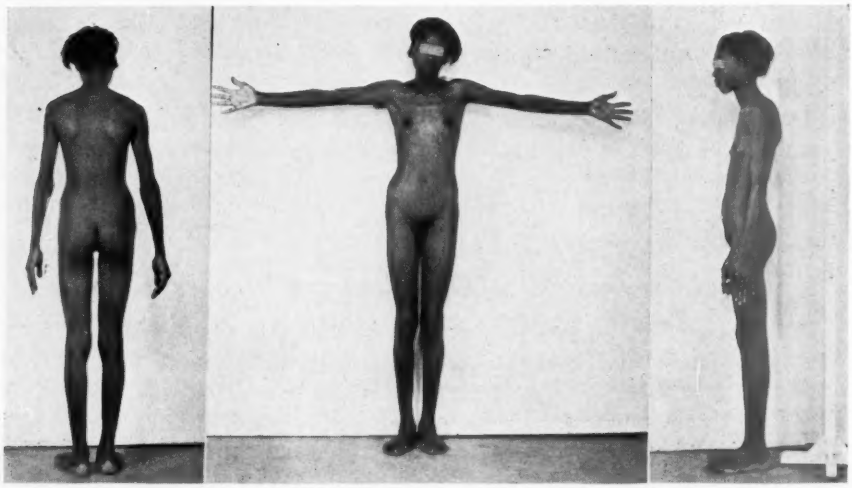

Fig. 1.—Patient 1, presenting typical statural and developmental signs of adolescent hypo-ovarianism.

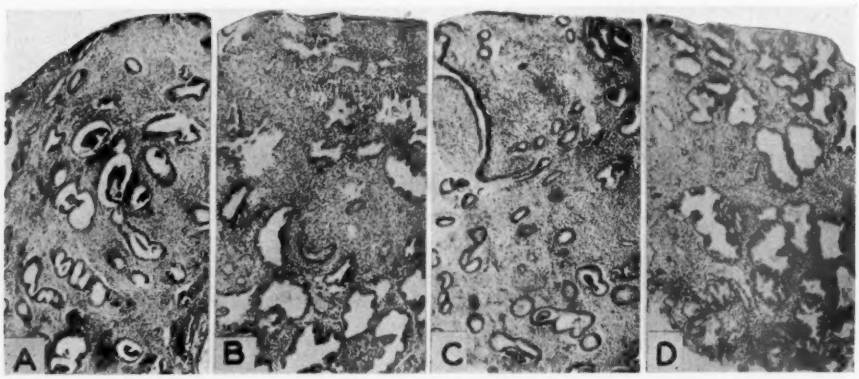

Fig. 2.—Endometrial responses of Patient 1.

The patient's treatment and her responses to it were as follows: She was given 100 R.U. of pituitary gonadotropins (maturity factor) every day for three weeks. During this therapy no significant responses occurred except a biphasic fluctuation in the leucocytes of the vaginal smears. Following this therapy she received 100 mouse units of equine gonadotropins (antex) every other day for twenty days, a total dose of 1,000 mouse units. After ten days of this treatment, a definite enlargement of the cervix and uterus was made out, and the left ovary was palpable for the first time, its size being estimated to be one-half inch in diameter. At the conclusion of this series of treatment, the ovary was thought to be cystic and to be about 1 inch in diameter. The right ovary was not felt. At the end of treatment the uterus measured 2 inches in depth and the cervix had changed from one of a flat character to a well-developed cone. A study of the biopsy of the endometrium

done at the conclusion of this series of therapy indicated a good estrogenic response (Fig. 2, *A*). A biopsy of the endometrium was impossible before treatment because of the marked uterine hypoplasia. No bleeding followed therapy or the biopsy. No therapy was given for the subsequent four weeks. Then a second series of equine gonadotropins was given over a period of six weeks. The patient received 3,400 mouse units of equine gonadotropins (antex), the individual dose being 200 mouse units. Increase in the size of the uterus occurred during this therapy so that at the end of therapy the uterus measured 2½ inches in depth. At the conclusion of therapy an endometrial biopsy was done, and study of the tissue obtained indicated a normal progestational endometrium (Fig. 2, *B*). Two days after the biopsy the first menstrual period of the patient began and lasted five days.

No further treatment was given. Twenty-six days after the onset of the patient's first period another endometrial biopsy was taken, the study of which showed a normal late estrogenic endometrium (Fig. 2, *C*). Fourteen days later another biopsy was taken. The endometrium secured at this time showed a good progestational response (Fig. 2, *D*). A menstrual period began the next day and lasted seven days. The subsequent course of the patient's bleeding was normal with cyclic menses continuing. Sexual maturation occurred rapidly. About 6 months after the patient's treatment ended, all the epiphyses were closed.

The next two cases to be presented are those of similar patients with classical adolescent hypo-ovarianism. These patients, however, failed to respond to equine gonadotropic therapy. Their dosage and its duration were far in excess of those given the first patient.

CASE 2.—Miss E. R., aged 19 years, was seen first in the Endocrine Division, July 10, 1939, because of delayed adolescence and menarche. Gynecologic and endocrine surveys yielded the following data: Axillary and pubic hair were essentially normal in amounts (having appeared four or five years previously). Breasts were of preadolescent hypoplastic nature. Feminine padding was minimum. Span exceeded height by 1½ inches while lower measurement exceeded upper measurement by 6½ inches. External genitalia were hypoplastic. Vagina was 10 cm. in depth. Uterus and cervix did not exceed 2 cm. in greatest dimensions. Ovaries were not palpable. Basal metabolism was –3 per cent. Roentgenogram of the skull showed the sella turcica to be normal. Osseous age estimated roentgenologically was delayed some several years, all epiphyses being open. Urinary titrations for sodium pregnanediol glucuronide and 17-ketosteroids (androgenic metabolic products) done daily for a period of fourteen days indicated the total excretion of the former during this time was 16 mg. and the average daily excretion of the latter was 18 I.U.

Therapy was initiated Aug. 3, 1939, and for the next ensuing six weeks the patient was given 200 I.U. of equine gonadotropins (gonadogen) and 300 R.U. of pituitary gonadotropins (maturity factor) every two days. No significant clinical responses were observed. A respite from therapy was allowed for six weeks. Beginning Oct. 27, 1939, and for the ensuing six weeks equine gonadotropins (anteron) were given every two days in amounts of 400 I.U. No significant clinical responses were observed. A rest period of eight weeks was given. Beginning March 11, 1940, and for the next ensuing six weeks the patient was given equine gonadotropins (anteron) in doses of 800 I.U. every two days. No evidence of ovarian stimulation was secured. On April 24, 1940, estrogenic therapy was initiated. For the next sixteen weeks the patient received estradiol dipropionate (di-ovocylin) 2.5 mg. (15,000 R.U.) every three days. During this therapy breasts increased to the areolomammary state and the uterus to two-thirds normal size. Beginning Aug. 22, 1940, similar therapy was initiated at two-day intervals and was to be continued for six weeks following which an additional trial of equine gonadotropins was to be made.

CASE 3.—Mrs. M. B., aged 26 years, para 0-0-0, was first seen in the Endocrine Division Aug. 2, 1939, because of delayed adolescent development and failure of menarche to occur. The patient gave a history of having had repeated basal

metabolism tests, the results of which had ranged from –32 per cent prior to therapy to –12 per cent under thyroid therapy. Endocrine and gynecologic surveys yielded the following data: Pubic and axillary hair were scanty, having appeared at about twelve to thirteen years of age. Breasts showed preadolescent hypoplasia. There was minimal feminine padding. There was a slight hypertrophy of the clitoris, otherwise the external genitalia were small. Vagina was of normal depth, but markedly narrow in its lumen. Uterus and cervix together did not exceed 1 cm. in greatest diameter. Ovaries were not felt. Span exceeded height by 4 inches. Lower measurement exceeded upper measurement by 11 inches. Basal metabolism was –13 per cent. Roentgenogram of the skull showed the sella turcica flat, but without evidence of erosion. Roentgenogram for osseous age evaluation indicated that all the epiphyses were open, the osseous age being estimated at sixteen years. Urinary titrations for sodium pregnanediol glucuronide and for 17-ketosteroids were done on 12 consecutive twenty-four-hour specimens. There was no excretion of sodium pregnanediol glucuronide. The average daily excretion of 17-ketosteroids was 27 I.U.

Therapy was begun Oct. 12, 1939, and for the next six weeks the patient received equine gonadotropins (anteron) 400 I.U. three times weekly. A month of rest from therapy followed. Beginning Jan. 11, 1940, and for the next four weeks the patient received equine gonadotropins (anteron) 800 I.U. three times weekly. No significant clinical responses occurred. One and one-half months of rest were given. Estrogenic therapy was begun April 22, 1940. The patient was given estradiol dipropionate (di-ovocylin) 2.5 mg. (15,000 R.U.) every two days for eight weeks. Definite enlargement of the breasts resulted. Slight enlargement of the uterus and cervix was observed. Estrogenic therapy was continued in the same dosage three times a week for another six weeks. Examination on Aug. 21, 1940, indicated continued adolescent development of breasts. The uterus was definitely enlarged to about one-half adolescent size. On Aug. 23, 1940, the patient had her first episode of bleeding. Following the conclusion of this episode of bleeding, the patient was started on cyclic gonadotropins (anteron). Responses to this therapy have not been evaluated as yet.

Despite intensive gonadotropic therapy of these two patients no significant ovarian responses occurred. It may be assumed that the ovaries of these patients were refractive, that they had not failed because of a pituitary deficit, but because of structural inadequacy and that, doubtlessly, the pituitary function of both was essentially normal.

The next case is reported because the patient failed to respond to pituitary fractions and equine gonadotropins over a period of four years, and then, after intensive estrogenic therapy, gave significant ovarian responses to equine and chorionic gonadotropic therapy. The patient lacks many of the characteristic stigmas of classical adolescent hypo-ovarianism as her record will indicate. The fact that she was of dwarfish stature seemed to justify our diagnosis of adolescent hypopituitarism, but she failed to respond to pituitary therapy until after adequate estrogenic therapy had been given.

CASE 4.—Miss S. R., aged 22 years, was seen first in the Endocrine Division Aug. 24, 1936, because of delayed menarche and statural retardation. Gynecologic and endocrine surveys yielded the following findings (Fig. 3): Moderately well-developed breasts and pubic and axillary crines; slightly hypoplastic external genitalia, a small juvenile cervix and uterus, ⅔ normal size; ovaries not palpable; increase in span over height of 2½ inches. The basal metabolism was –3 per cent. Roentgenograms of the sella turcica were negative. Osseous age was estimated roentgenologically at thirteen to thirteen and one-half years. An endometrial biopsy secured hypoestrogenic (atrophic) endometrium.

The early therapeutic record of the patient was as follows: Pituitary gonadotropins (maturity factor) and posterior pituitary extract (obstetrical pituitrin)

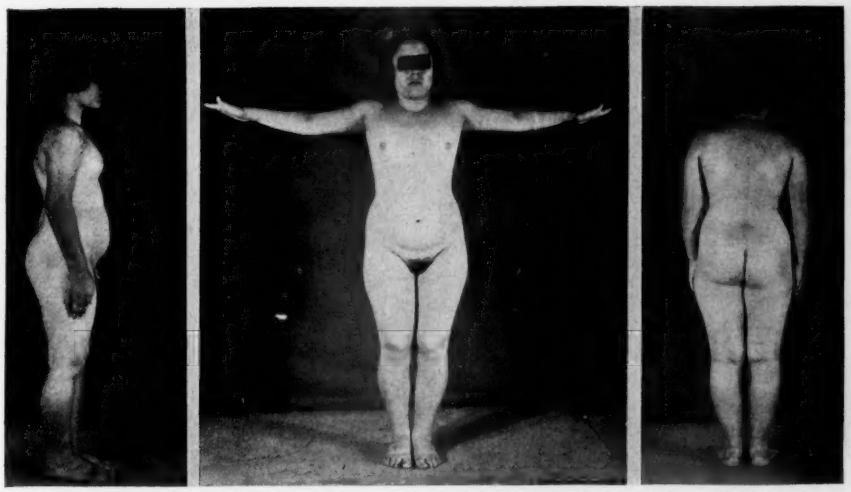

Fig. 3.—Statural and developmental status of Patient 4.

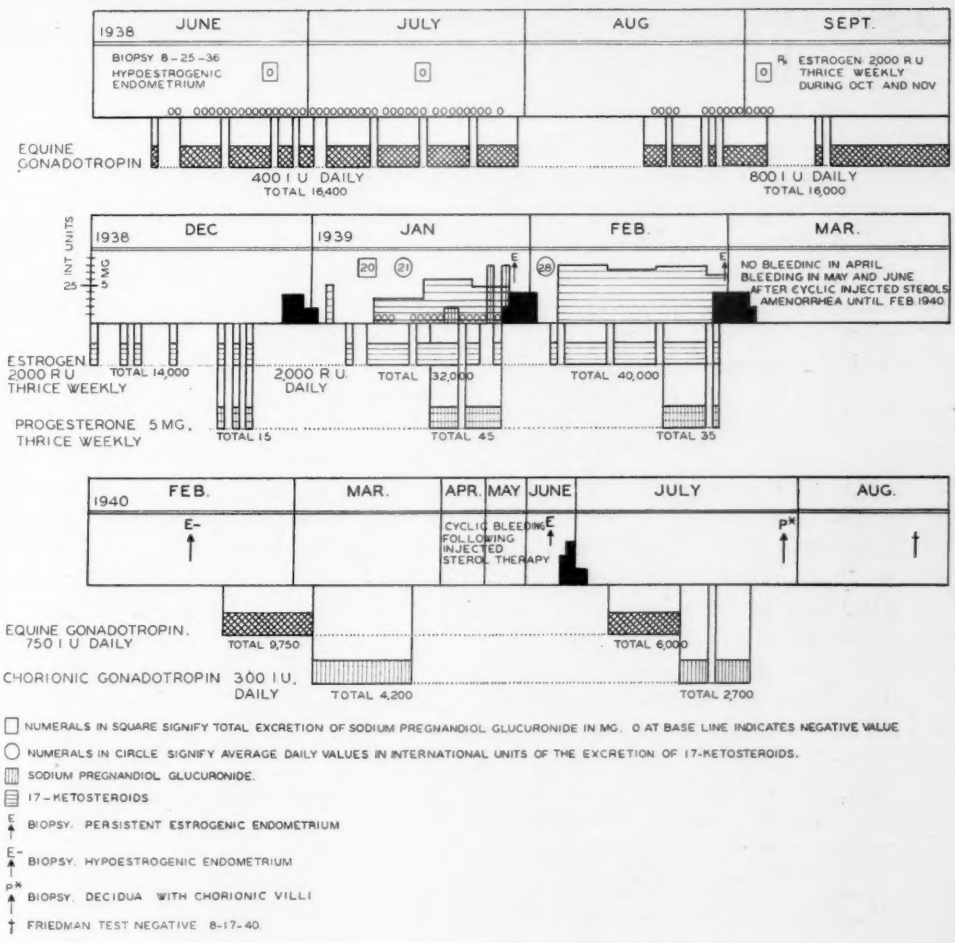

Fig. 4.—Therapeutic and progress record of Patient 4.

were given in doses of 2 c.c. and 0.5 c.c., respectively, three times weekly from Aug. 28, 1936, to Sept. 30, 1936. At this time posterior pituitary extract was discontinued and the pituitary gonadotropin was continued until Dec. 14, 1936. No clinical responses were observed. From Dec. 14, 1936, to March 1, 1937, an unfractionated anterior pituitary extract (polyansyn) was given in doses of 2 c.c. three times weekly. No clinical responses occurred. From March 1, 1937, to June 9, 1938, no treatment was given the patient except small amounts of thyroid substance and estriol glucuronide (emmenin). No significant clinical responses occurred.

The remainder of the patient's therapy and ovarian responses are given in Fig. 4. During the four years of observation and treatment, the patient gained approximately 1 inch in height and 1½ pounds in weight. Epiphyseal age advanced to normal.

The striking observation in this case is that no significant responses occurred to treatment with gonadotropins until uterine growth and proliferation and cyclic bleeding had been produced by intensive cyclic sterol therapy (embracing estrogens and progesterone) and until the combined use of equine and chorionic gonadotropins was instituted. This patient's record would seem to indicate that receptivity of the ovaries to pituitary stimuli may be in some way associated with the adequacy of endometrial function. This association may be by way of the reciprocities of the ovaries and the endometrial metabolism of sterols. It certainly suggests the advisability of repeated therapeutic tests of gonadotropic therapy in patients of this type after uterine growth and endometrial priming have been obtained from sterol therapy.

No doubt exists in our minds concerning the completeness of the ovarian response of this patient since a pregnancy occurred as the immediate result of gonadotropic therapy. This was proved by an endometrial biopsy which secured chorionic villi. No bleeding followed this biopsy. No subsequent abortion occurred. It may be assumed that the product of conception was removed by the biopsy forceps. The patient has had amenorrhea from June until the present time (October). There has been no uterine enlargement indicative of continued pregnancy.

THE TREATMENT OF FUNCTIONAL UTERINE BLEEDING

We have been unable to rely upon gonadotropic therapy to regulate acyclic flowing. Even when specific ovarian responses, as judged by endometrial findings, have followed this form of treatment, cyclic bleeding frequently did not ensue and, in fact, on some occasions no bleeding occurred. We have been impelled, therefore, to employ frequently cyclic sterol therapy for the regulation of bleeding, reserving the use of gonadotropins for attempts at pregnancy in those patients in whom attendant sterility was undesired.

Ten young women, whose ages ranged from 16 to 31 years, and whose common menstrual symptom was amenorrhea, primary in 7 instances, were treated, each with one or more series of equine gonadotropins. None of these patients bled during or following therapy. No significant ovarian or endometrial alterations were observed.

Since our results with gonadotropic therapy which embraced the use of equine gonadotropins alone had not been encouraging either from

the point of view of subsequent ovarian responses or as judged by regulatory effects on acyclic bleeding, a system of combined therapy employing both equine and chorionic gonadotropins in one-two order was devised.[9] In this system equine gonadotropins were administered daily during the first ten days of treatment (beginning on the fifth or sixth day of the bleeding cycle, if one existed) and chorionic gonadotropins were given daily during the last ten days of treatment. An interval of seven days following conclusion of therapy was reserved for bleeding. Following this interval another series was given, if it was deemed advisable. (The details of this form of therapy, including dosages employed, are presented in the graphic charts of Cases 4, 5, 7, and 8.)

The most satisfactory results we have secured from any form of gonadotropic therapy have followed this combined one-two system. Nineteen young women, whose ages ranged from 14 to 31 years and whose common gynecologic complaint was menometrorrhagia, related by diagnostic studies to estrogenic bleeding (failure of ovulation) were treated by this system. Five of these women responded specifically to this therapy, as judged by the induction of progestational differentiation of their endometria. It should be reported that only 2 of these 5 patients continued to bleed from progestational endometria following discontinuation of treatment. The remaining 3 experienced a return of acyclic estrogenic bleeding.

Nine young women, whose ages ranged from 25 to 36 years, and whose common gynecologic complaint was oligomenorrhea related by diagnostic studies to estrogenic bleeding, were treated similarly. Three of these women responded specifically to this therapy as judged by the occurrence of progestational differentiation of their endometria. One of these experienced a return of estrogenic bleeding of oligomenorrheic character after treatment was discontinued. One became pregnant. The follow-up record of the other one is lacking.

These data indicate that even in the small group of patients, in which positive ovarian responses follow therapy, the cure of their ovarian failure is not necessarily permanent. It is no doubt true that, when hypopituitary function is the cause of ovarian failure, continued substitution at the pituitary level is just as necessary to maintain fertile cycles as continued substitution at the ovarian level in patients with primary ovarian failure is to maintain cyclic bleeding. Continued substitution at the pituitary level with our present commercial preparations is impossible not only because of cost, but also because of antibody formation and consequent phenomena of inverse responses.

The exact modus operandi of this one-two system of combined gonadotropic therapy is not known. It has the support, however, of the studies on monkeys of Engle and Hamburger[10] who found a similar therapeutic regime necessary for specific ovarian responses. Büttner[11] has had similar clinical experiences.

The following case is cited because it illustrates the fact that the cyclic employment of sterols and of gonadotropins often is necessary for the complete handling in functional menometrorrhagia.

CASE 5.—Mrs. M. O., aged 26 years, para 0-0-0, was first seen in the Endocrine Division Oct. 24, 1939, because of metrorrhagia of eight months' duration. The patient gave a history of recurring episodes of oligomenorrhea, cyclic menses and metrorrhagia since her menarche at 13 years. Gynecologic and endocrine surveys showed nothing particularly unusual except for symmetrical obesity. Basal metabolism was +4 per cent. The menstrual irregularity was treated by curettage followed by cyclic employment of oral sterols for four months. Cyclic bleeding resulted. Biopsies of the endometrium taken at the onset of these episodes of bleeding all indicated estrogenic bleeding.

Therapy with cyclic gonadotropins was begun June 2, 1940. Fig. 5 presents graphically the details of this therapy and the endometrial responses to it.

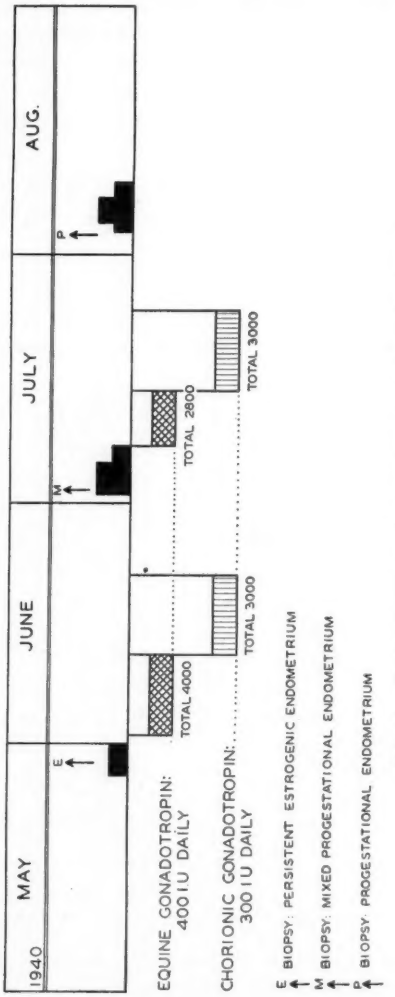

Fig. 5.—Therapeutic and progress record of Patient 5.

TREATMENT OF OVARIAN STERILITY ASSOCIATED WITH CYCLIC BLEEDING

Three women whose ages ranged from 25 to 40 years and whose symptoms included ovarian sterility and cyclic bleeding were treated with 1 or 2 series of cyclic equine gonadotropins. None of them became pregnant. One of these women illustrates the definite existence of ovarian

refractivity. This is relatable doubtlessly to the climacteric process, as the patient was 40 years of age. Her case record follows:

CASE 6.—Mrs. A. G., aged 40 years, para 0-0-0, was seen first in the Endocrine Division July 5, 1939, because of her inability to conceive during her eight years of marriage, during six of which no contraception had been practiced. Endocrine and gynecologic surveys indicated no apparent cause of the patient's sterility except

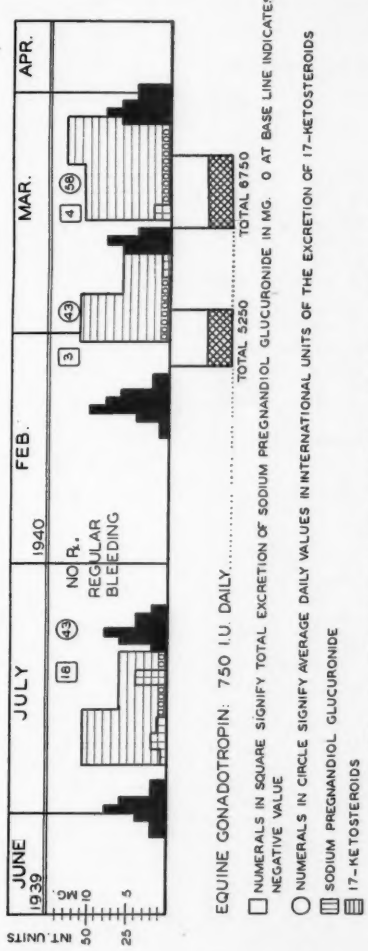

Fig. 6.—Therapeutic and progress record of Patient 6.

an acute angulation of the cervix and ovarian failure as indicated from the hormonal titrations presented graphically in Fig. 6. The acutely angulated cervix made endometrial biopsy impossible. The patient's basal metabolic rate was −1 per cent. Tubes were patent when examined by uterosalpingography with lipiodol. The husband's urologic and endocrine surveys were negative.

Two cyclic series of equine gonadotropins failed to remedy the ovarian failure as judged by urinary titers of sodium pregnanediol glucuronide (Fig. 6).

Three patients with ovarian sterility and cyclic menses were treated with combined one-two gonadotropic therapy. All 3 of these patients became pregnant promptly, in fact, during the first series of treatment. The case records of 2 of these patients are presented.

CASE 7.—Mrs. L. R., aged 33 years, para 3-3-0, was seen first in the Endocrine Division Sept. 2, 1937. During the patient's previous five years of marriage, 3 abortions had occurred at approximately the third month of gestation. Endocrine and gynecologic surveys were essentially negative except for clinical hypothyroidism. The patient's basal metabolic reading when seen first was –21 per cent.

During a two-and-one-half-year period of study no pregnancy occurred, despite the fact that metabolic irregularities were adjusted by thyroid substance to full clinical tolerance. These studies, presented in part in Fig. 7A, indicated ovarian failure which was not overcome by thyroid therapy.

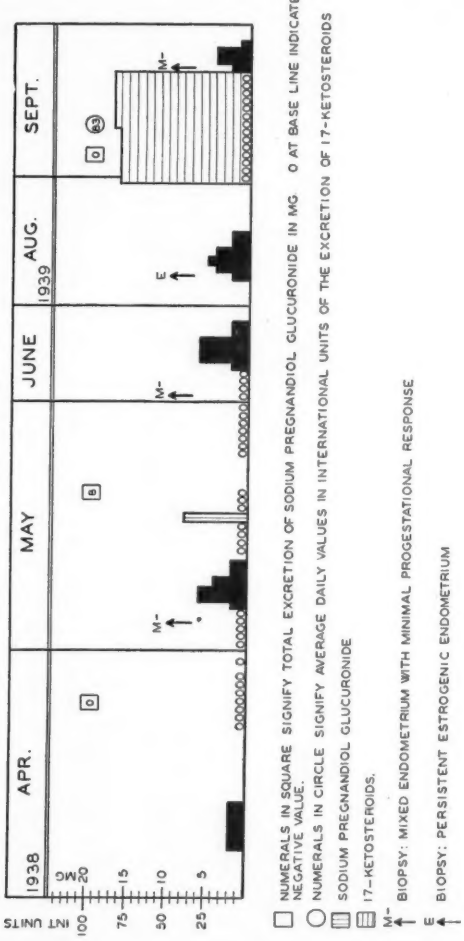

Fig. 7A.—Record of diagnostic studies of Patient 7.

On April 22, 1940, a series of combined gonadotropic therapy was instituted which led to a pregnancy. Fig. 7B presents graphically the clinical record from this time on, including therapy and urinary titrations for 17-ketosteroids and sodium pregnanediol glucuronide. This record covers the cycle preceding pregnancy, the pregnancy and the patient's spontaneous abortion July 30, 1940.

CASE 8.—Mrs. M. McC., aged 25 years, para 0-0-0, was seen in the Endocrine Division July 11, 1939, because of inability to conceive during her five and one-half years of marriage. She had had previously various diagnostic procedures, but no endocrine investigations or therapy except thyroid substance. The patient's last sterility investigation had included a tubal insufflation about two and one-half years previously.

Despite the fact that the patient gave a history of marked oligomenorrhea since menarche at 15 years of age until approximately one and one-half years previously, endocrine and gynecologic surveys were essentially normal. Roentgenogram of the skull was negative. Basal metabolism was −12 per cent.

The endocrine investigation of this patient, as well as the patient's therapy which resulted in pregnancy and the course of this pregnancy, which was threatened by abortion, are given in Fig. 8.

The only special investigative procedures done by us included quantitation of urinary titers and endometrial biopsy. No tubal insufflation was done.

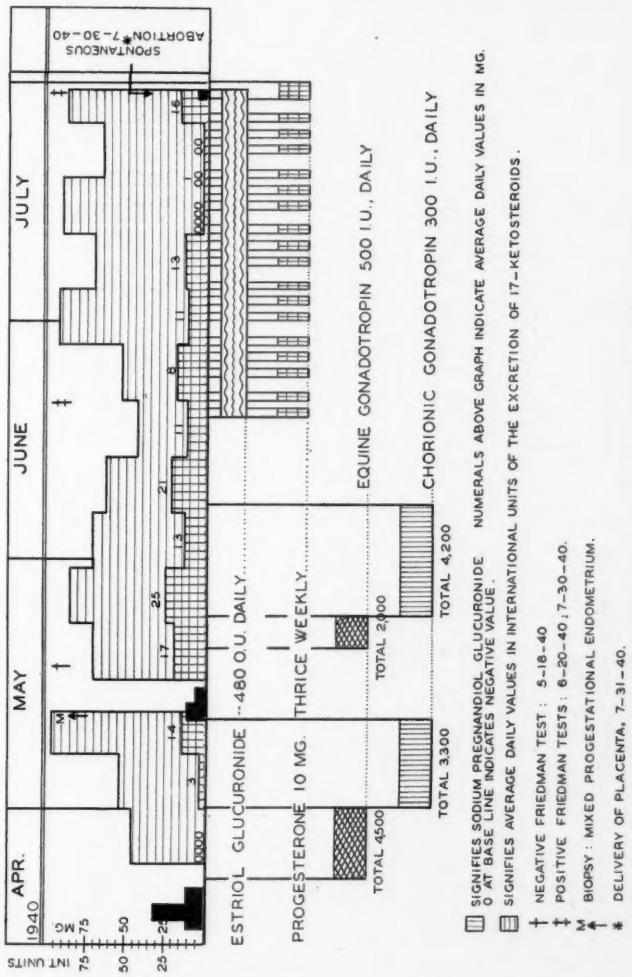

Fig. 7B.—Therapeutic and progress record of Patient 7.

It is interesting to note the obstetric history of the two patients presented: One threatened to abort; the other aborted. Abortion occurred in Patient 7 despite intensive therapy instituted at the onset of pregnancy designed to circumvent any ovarian failure during the ovarian phase of pregnancy.

These observations indicate that incurrent ovarian failure should be anticipated during early months of pregnancies in women in whom ovarian sterility was circumvented temporarily by gonadotropic therapy.

COMMENTS

We are convinced that there is a limited role in gynecic therapy for the gonadotropins. The use of gonadotropins is not the therapeutic solution to the majority of instances of ovarian failure.

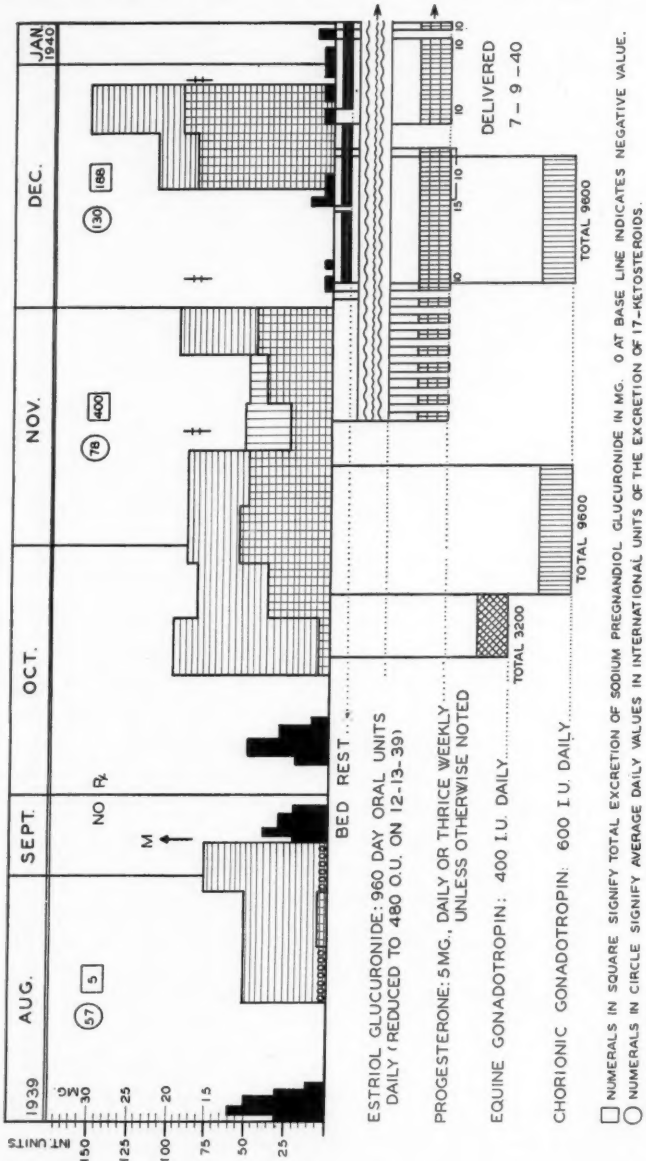

Fig. 8.—Diagnostic, therapeutic, and progress record of Patient S.

It continues to be our belief that only in those instances in which there is definite pituitary failure are these substances of any therapeutic value. Once the pituitary failure has been overcome by this therapy, the ovarian adjustment may be often only temporary. At the present time it is impossible to carry out any long time substitutional therapy

for pituitary failure. Such therapy under favorable circumstances should be reserved for well-timed attempts to circumvent undesired sterility of hypopituitary origin.

Since it is impossible frequently to diagnose hypopituitarism, especially of a functional nature, it often becomes necessary to give patients a therapeutic test of gonadotropic therapy. This test should have finite objectives and limits. Treatment should not be prolonged indiscriminately when no responses are occurring. Likewise treatment should not be given without ample rest periods, even when responses are being obtained, for fear of antibody reactions.

Except in a few isolated instances of patients with adolescent hypo-ovarianism, our therapeutic results with the use of equine gonadotropins alone have been and continue to be extremely disappointing. The combined cyclic employment of both equine and chorionic gonadotropins in the one-two manner described by us has yielded significant specific responses in a minority group of patients with ovarian failure. These observations apparently indicate that equine gonadotropins alone are incapable of providing complete substitutional therapy in instances of hypogonadotropic failure of the pituitary. The modus operandi of the one-two combined therapy is not known. It may take advantage of a necessary synergism or it may afford critical alterations in sterol levels, especially those of estrogens, which are necessary for ovulation. The chorionic portion of the therapy doubtlessly tends to amplify and augment corpus luteum function, once ovulation has occurred.

Patients with classical adolescent hypo-ovarianism should be given a trial of equine gonadotropic therapy. If negative responses are given, intensive estrogenic therapy should be instituted, and from time to time the patient should be given other trials of equine gonadotropic therapy. Apparently in some instances ovarian receptivity is increased by the production of uterine and endometrial proliferation, resulting from sterol therapy. Unless complete ovarian responses can be initiated in these individuals, the establishment of complete ovarian function, compatible with fertility, is impossible.

In patients with oligomenorrhea, amenorrhea, and menometrorrhagia of functional nature, associated with undesired lowered fertility or sterility, it is often necessary to initiate and maintain cyclic bleeding with ovarian sterols while patients are being tested with cyclic gonadotropic therapy in attempts to secure pregnancies.

There is little need or rationale for the use of gonadotropins in women of climacteric age. The ovaries of these women are intrinsically refractive, and their pituitaries are either functioning normally or at higher levels than normal.

When pregnancies are salvaged from women with ovarian sterility by gonadotropic therapy, abortion or miscarriage is likely to occur from intercurrent ovarian failure. It is our opinion that each of these patients should be handled as though she gave a history of having had previous abortions.

SUMMARY

1. Equine gonadotropins may stimulate ovaries which possess normal sensitivity to pituitary stimuli.

2. Equine gonadotropins are of value therapeutically in those women whose ovarian failure is due to deficient pituitary function.

3. The effects of equine gonadotropins are often temporary, the pituitary failure and the secondary ovarian failure recurring.

4. This last statement has a bearing upon the handling of pregnancy secured by this form of therapy. Intercurrent ovarian failure and abortion should be anticipated and prophylactic treatment instituted.

5. The combined one-two employment of equine and chorionic gonadotropins has proved more effective than the use of cyclic equine gonadotropic therapy alone.

6. Cyclic gonadotropic therapy in our hands fails to insure cyclic bleeding, thus indicating inadequate production of complete ovarian responses.

7. Equine gonadotropic therapy is only one of the methods available for the treatment of ovarian failure.

We acknowledge our indebtedness to the following commercial organizations for liberal quantities of specified ones of their preparations supplied for these studies: Ayerst, McKenna & Harrison, Montreal, Canada, maturity factor, polyansyn, emmenin, antex (Leo), APL; Ciba Pharmaceutical Products, Inc., Summit, New Jersey, diovocylin; Cutter Laboratories, Berkeley, California, Gonadin; Schering Corporation, Bloomfield, New Jersey, anteron; Upjohn Company, Kalamazoo, Michigan, gonadogen.

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DISCUSSION

DR. M. EDWARD DAVIS.—In experimental animals of a half dozen species, equine gonadotropin will substitute completely for the anterior lobe of the pituitary gland. It will produce follicle growth, luteinization and normal ovulation. Ova released from their follicles artificially can be fertilized and will develop in normal young. A major difficulty in the application to human problems is the diagnosis of the character of the glandular failure resulting in clinical manifestations, and it is therefore not surprising to find that equine gonadotropin does not always prove efficacious in medical practice.

Our experience indicates that in some adolescent and underdeveloped individuals with primary amenorrhea good results can be obtained by gonadotropic therapy. These young women mature and develop regular cyclic bleeding. In some, however, gonadotropic therapy is a complete failure. Probably in these individuals the primary amenorrhea is the result of ovarian failure, the pituitary being normal.

We have been more successful in the treatment of patients with secondary amenorrhea. In more than one-half of the individuals in this group, it has been possible to produce regular cyclic bleeding by means of equine gonadotropin. It has likewise been possible to demonstrate ovulation by endometrial biopsies in many instances.

Equine and chorionic gonadotropins may well complement each other in producing a more desirable effect. The chorionic substance has little follicle-stimulating effect and consists largely of a luteinizing action. There is thus a very marked biologic difference between these two gonadotropins.

Equine gonadotropin is not a panacea for the treatment of all menstrual irregularities. There is still much to be learned concerning the proper dosage, the time interval, and the mode of administration. Until such a time as a pure principle can be isolated from the anterior lobe, equine gonadotropin appears to be the most potent gonadotrope.

DR. ARTHUR K. KOFF.—In the past Dr. Hamblen has proved to be an iconoclast with regard to the therapeutic value of gonadotropic hormones. For example, he was the first to prove conclusively that gonadotropic hormones derived from pregnancy urine have no effect on the human ovary except perhaps to produce atresia of the follicles.

Most of us who have worked with pregnant mare serum hormone fully agree with Dr. Hamblen that much more well-controlled clinical work must be done before we can prove or disprove its therapeutic value.

Experimentally the following facts with regard to the pregnant mare serum hormone have been established:

1. That both the follicle-stimulating and luteinizing gonadotropic factors are present; and consequently will produce in the ovaries of hypophysectomized laboratory animals follicle growth, ovulation, corpus luteum formation, and luteinization of mature follicles. Therefore, the pregnant mare serum hormone has the same influence on the ovary as pituitary implants or combinations of gonadotropic hormones derived from menopausal urine and pregnancy urine.

2. That the pregnant mare serum hormone is not excreted by the kidney and appears to be utilized or destroyed slowly so that a prolonged or sustained effect on the ovary occurs regardless of the route of administration.

3. That both in primates and the human intravenous administration of suitable doses of pregnant mare serum hormone will induce or hasten ovulation in the normal ovary. Theoretically then, this gonadotropic preparation should be effective particularly in those instances of hypo-ovarianism associated with pituitary failure, e.g.: amenorrhea, oligomenorrhea, and failure of ovulation. Actually in my own experience the results have been inconsistent and disappointing. For example, I have studied 21 patients with anovulatory cycles, the diagnosis having been established on the basis of repeated endometrial biopsy. To date only 3 of these patients have ovulated with pregnant mare serum hormone therapy, and I am not certain that they might have ovulated without stimulation. It is quite interesting that in this group there were 11 instances of hypothyroidism or let us say hypometabolism, with basal rates of ten or below. Eight of the eleven that showed hypometabolism began to ovulate within six weeks to three months after thyroid therapy was started. Ora Sevringhaus of New York has shown that when the thyroid is removed from laboratory animals there is a rapid disappearance of the acidophile cells of the anterior hypophyses, and it is possible that the acidophile cell is responsible for the elaboration of the luteinizing hormone. Reasoning from his observations, we can assume that a patient with decreased thyroid function probably may very well develop hypopituitarism and consequent ovarian failure.

I am very much interested in the results obtained by combining pregnant mare serum and pregnancy urine gonadotropic hormones in sequence. I remember that Büttner in 1937 described ovulation in the human female by the use of combined pituitary and pregnancy urine gonadotropic hormones explaining that the follicle-stimulating hormone prepared the follicle and the luteinizing hormone added the stimulus necessary to produce ovulation. He termed this the one-two reaction comparable to the estrogen-progestin effect on the endometrium.

DR. R. R. GREENE.—My own clinical experience with equine gonadotropin has been uniformly unsuccessful. I have secondarily observed some work being done by Dr. Brewer and Dr. Skiles. They administered to individuals with normal menstrual cycles and presumably normal ovaries doses of gonadotropic hormone, varying from

250 to 7,000 international units. These patients were then operated upon one to five days after the last dose was given. Dr. Brewer informs me that in only one individual was there a corpus luteum present that was probably caused by the therapy.

The matter of dosage is very important. In the rat, Cole and Sanders, in 1932, noticed that with very low dose you got either no effect or slight stimulation. A high dose produces ovulation with corpora lutea. With just a little higher dose, there is apparently a rather rapid luteinization with the ovum wrapped within the corpus luteum.

During a certain season of the year in North America the monkey normally has anovulatory cycles. To 104 such animals Hartman gave equine gonadotropic hormone. Of these, 7 had a normal corpus luteum. In 32 animals there was absolutely no effect on the ovary, with just the same dose. In 16 there was a definite temporary damage to the ovary, consisting in the production of multiple large follicles which did not ovulate.

Superovulation has been produced in the rat with equine gonadotropin so that 18 to 20 young will be born instead of the 6 to 10 as normally. In the last year we have been trying to repeat these experiments and have treated 283 rats with the accepted dosage. None of our animals had over 10 offspring. This is not because we have not used potent equine gonadotropin, but no doubt because our rat colony is different from others.

These are illustrations of how important dosage is in experimental animals, but dosage is much easier to control in experimental animals than in the human being. I am wondering if some of the poor results in the human being are not due largely to the fact that the right dosage was not given. I can make no suggestion on how to decide what is the right dosage.

Dr. Hamblen presented cases which had fairly good progestional response in the endometrium and little or no pregnanediol in the urine. This brings out a point that should be mentioned. The present concept of pregnanediol is that it is very specific in a quantitative way as an indicator of the function of the corpus luteum in the human being. Dr. Hamblen's examples show that this is not necessarily true. Progesterone in its metabolism may be broken down into a good many products.

DR. HAMBLEN (closing).—A summary of our system of one-two gonadotropic therapy is as follows: On the fifth to the seventh day of the cycle (or upon conclusion of bleeding), the administration of equine gonadotropins is begun. The daily dosage has been 400 to 800 international units, given intramuscularly. Treatment continues for ten days (i.e., until the presumed time for ovulation). Immediately following the series of equine gonadotropins, chorionic gonadotropins in daily doses ranging from 500 to 750 international units are given for ten days. Therapy is discontinued if bleeding begins before the entire series has been given. If a positive endometrial response (progestational endometrium or pregnancy) follows this therapy, further treatment is not given and only is it repeated at infrequent intervals if there is a return of former pretreatment level of ovarian failure. If a negative response following therapy occurs, one more trial of it is made the next cycle.

Dr. Koff has mentioned Büttner's work (Arch. f. Gynäk. **163:** 32, 1937) which was not referred to in my paper. Likewise, I made no reference to Engle's important study (Endocrinology, **18:** 513, 1934; and with Hamburger, Proc. Soc. Exper. Biol. & Med. **32:** 1531, 1935) on monkeys. Both these workers found a one-two system of gonadotropic therapy effective in inducing ovulation. Engle's observations indicated a necessity for the dual action of these two types of gonadotropins in order to induce complete ovarian responses in the monkey. (Büttner also secured ovulation from chorionic gonadotropins alone.) The explanation of the required duality of action probably lies in the necessity of "synergizing" or "augmenting" the action of equine (or follicle-stimulating hormone) gonadotropins with chorionic (or pregnancy urine) gonadotropins. Our observations lead to the belief that in the case of woman (as well as that of the monkey) equine gonadotropins do not constitute a "complete" gonadotropic principle; in women, however, with normal pituitary-ovarian reciprocities equine gonadotropins may be "synergized" or "augmented" by the pituitaries of these patients and, thereby, prove capable of inducing ovulation.

Dr. Greene has questioned if we know the effective dosage of these gonadotropins. I am sure that we do not, certainly not the minimal dosage requirements. These are conditioned, doubtlessly, by the degree of pituitary failure existing. We shall probably not be able to calculate dosage accurately until we are able to diagnose and grade pituitary failure with some degree of certainty. In some of our patients, I feel sure we have too large doses, i.e., hyperluteinized the ovaries; for instance, in those patients who yielded progestational responses but failed to bleed subsequently.

Time will not permit my answering satisfactorily Dr. Greene's question as to our opinion of the clinical significance of urinary pregnanediol. I can state only that we regard its quantitation to be a means of studying corpus luteum function, but one which does not tell the whole story and often only a small part of the story and that also we have found this study to be of little or negative value in regard to the utilization and metabolism of injected progesterone.

MENSTRUATION AND URINATION THROUGH A CLITORISLIKE STRUCTURE*

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M. B., a 21-year-old white female, was admitted to the gynecologic service on May 4, 1939, after having had a complete urologic work-up in the Urological Department. The complaints presented at this time were: (1) urination and menstruation through a penislike organ; (2) dysmenorrhea; (3) inability to have intercourse; and (4) certain psychic disturbances because of her functional deformity.

Abnormality was noted at birth, but due to the opinion of the attending doctor and the parents, nothing was done about the condition.

Menstruation began at 13 years. Periods were regular, lasting from three to four days. Periods were always painful, as were the two days prior to their onset. The menstrual flow presented itself from a clitorislike structure through which the patient normally urinated. Urine during menstruation always appeared blood tinged.

Patient had bothered little about her condition until recently, when she was made conscious of her differences from other females by the attempt of her fiance to have intercourse with her. This embarrassed her and caused her to feel very inadequate. The dysmenorrhea had recently become more severe than before.

Physical examination at the time of admission revealed a well-developed, well-nourished white female of 21 years, presenting normal secondary sex characteristics, mammary glands and hair distribution. The urethral orifice emptied from a penislike structure 3 cm. long and 1½ cm. in diameter, this urinary passage being formed by the fused labia minora, which were continuous with this clitorislike structure above. The remainder of the physical examination was essentially negative.

Cystoscopic examination revealed a normal though small vagina with an infantile cervix about 12 cm. distant from the introitus; on the anterior wall of the urinary passage about 4 cm. distant from the lower end of the true vagina the true urethra emptied. These structures were surrounded externally by skin resembling the prepuce in the male. Below was a sealed cleft surrounded by normal labia majora. The uterus was palpable rectally. The bladder was normal. Both uretheral orifices were visualized, and a ureteral catheter was passed on the right and a retrograde pyelogram made.

*Presented at the New York Obstetrical Society, October 8, 1940.

X-rays showed a questionable congenital anomaly of the kidneys, spina bifida occulta and pelvic disproportion with incomplete fusion at the symphysis pubis, following the rule that congenital anomalies are often multiple.

Urine was negative; blood count, normal; Wassermann, negative.

Operative Procedure.—On May 5, 1939, under gas-oxygen-ether anesthesia, a slightly bent-grooved director was introduced into the combined urinary and vaginal orifice with the point toward the perineum. The skin and underlying tissues which were about 3 cm. thick over the lower end of the vagina were cut in the midline down

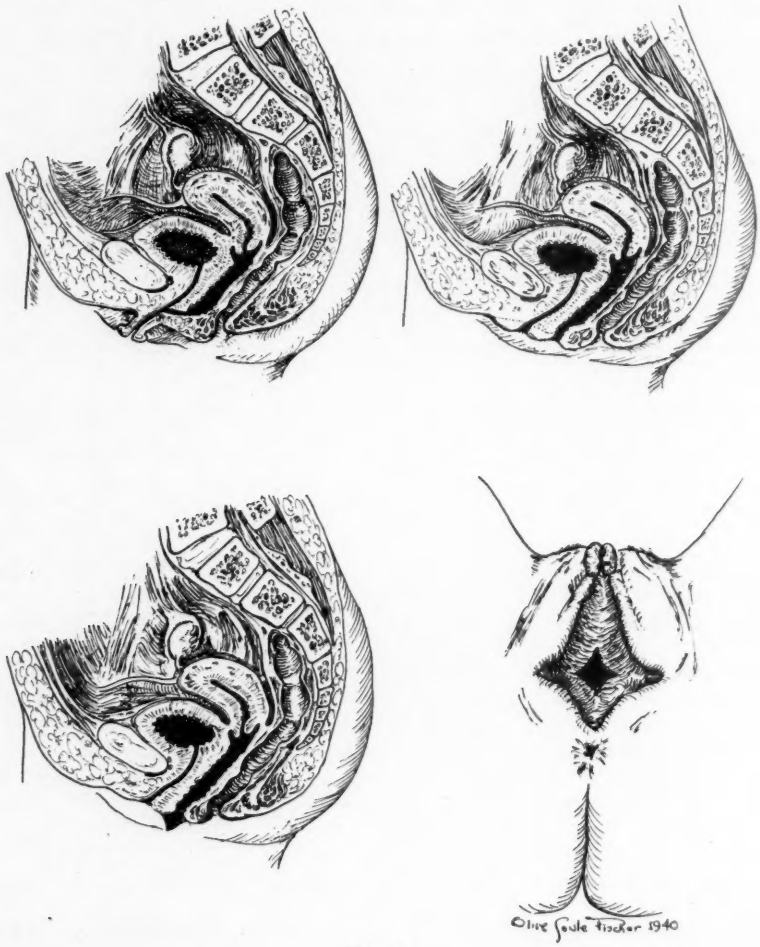

Fig. 1.

to the grooved director, thus laying open the passage and the true opening of the vagina, which admitted scant 2 fingers. This incision was extended down to the anterior border of the sphincter ani muscle. The cut vaginal mucous edges were sutured to the cut skin edges on either side with interrupted sutures of plain catgut. A small wick was placed in the vagina for drainage.

The patient enjoyed an uneventful convalescence and was discharged on May 11, 1939. During her stay she received the usual sedatives and urinary antiseptics to minimize an ascending urinary infection.

Patient returned to the Clinic for weekly vaginal dilatation. However, after several months it was decided that a bilateral episiotomy would accomplish dilata-

tion of the vaginal introitus more favorably. This was done on July 20, 1939, and the patient was discharged one week later in good condition.

This case is of interest because of its infrequency; according to Engstad,[1] one in 5,000 have a similar condition.

The embryologic background of this case is interesting. In a recent article on the formation of pelvic viscera by E. Levy,[2] it is pointed out that the entire process of development of the external genitalia in the female is accompanied by fewer structural changes than occur in the male. Completion of development takes a longer time, so that final differentiation in the female does not synchronize with the more differentiated transformation in the male. The genital groove, however, is shorter. The groove on the tubercle becomes obliterated and the genital folds separate from the groove. Characteristic of the female is the caudal decurvation which appears to be brought about by an excess growth of the cavernous over the urethral regions of the phallus. The urethral folds develop as caudal projections supporting the slightly overhanging glans, which become more clearly defined than in the male. The caudal ends of the labioscrotal swellings grow toward each other and join in the midventral line to form the posterior commissure. In this manner these originally paired swellings are transformed into a cranially opened, horseshoe-shaped rim, enclosing the external genitalia and separating them from the anus. The labioscrotal swellings form the labia majora. The shaft and glans of the phallus form the clitoris, and the ununited urethral folds separate from the clitoris, and become the labia minora. In the case just reported, these urethral folds united and failed to separate from the clitoris, giving the previously described deformity. Normally the unobliterated urogenital orifice becomes the urethrovaginal orifice. The prepuce is formed as in the male, but its growth is slower and generally less marked than in this instance.

The menstrual function has been normal since leaving the hospital and coitus satisfactory. Examination August, 1940, revealed ample two-finger plus introitus with ample vagina.

In summary, a case of anomalous development of the female external genitalia is presented, the indications for operation given, the operative procedure employed described, and a brief summary of the embryologic background given.

Undoubtedly this deformity arose from imperfect canalization of the lower end of the Müllerian ducts, as the layer of tissues overlying the lower end of the true vagina, showed a thickness up to 3 cm., much more than would be explained by a simple imperforate hymen. The other congenital abnormalities indicate that it was a major rather than a minor deviation in such as is frequently reported as adherent labia minora.

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130 EAST 56TH STREET

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Experience at the Boston City Hospital during the last three years has convinced the writers that a technique, based on the method of Ball of Columbia University, is simple, inexpensive, informative, and practicable for general use.

X-ray pelvimetry should not supplant external and internal measurements and palpation, but should supplement them in questionable cases.

HUGO EHRENFEST.

AMENORRHEA AND STERILITY CAUSED BY BILATERAL POLYCYSTIC OVARIES*

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IN 1934, Stein and Leventhal described a syndrome characterized by amenorrhea and sterility associated with bilateral polycystic ovaries, and reported 7 patients treated by wedge resection. The importance of the associated findings was amplified in a recent paper by Stein and Cohen (1939) who described the subsequent course in the previously reported patients and added 22 additional cases. The following case report is a striking example of the role of bilateral polycystic ovaries in the causation of amenorrhea and sterility and adds incontrovertible evidence for the presence of this clinical entity.

CASE REPORT

Mrs. B. S., aged 26 years, consulted me on Dec. 4, 1935, complaining of amenorrhea of three years' duration and sterility of one year's duration. Menstruation began at 13 years of age and was irregular with intervals ranging from one to two months until the onset of the amenorrhea. The duration of the menses was five

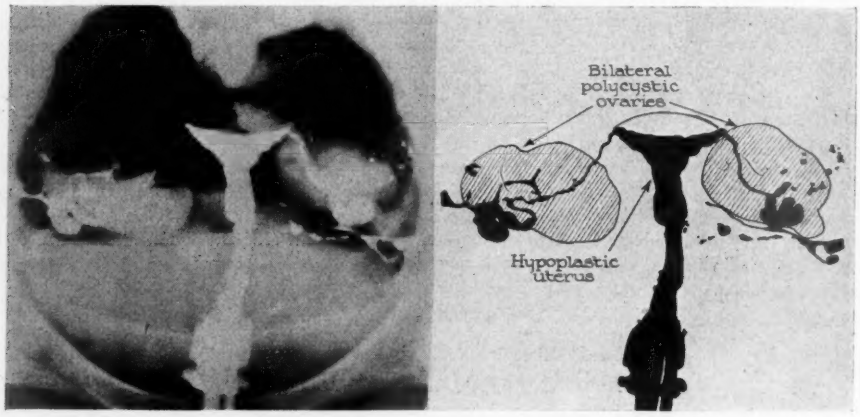

Fig. 1.—Transuterine pneumoperitoneum with lipiodol instillation. Bilateral polycystic ovaries with uterine hypoplasia. "Spill" demonstrates tubal patency.

days, the amount moderate, and there was an associated slight dysmenorrhea. There had been only one menstruation since marriage three and one-half years previously. The past history was negative, except for scarlet fever and influenza. Physical examination revealed a normal-appearing well-nourished female who weighed 135 pounds. The breasts were well developed, and there were no stigmas of masculinization. The external genitalia were normal. On bimanual examination, the uterus was found to be small, freely movable, and in second-degree retroversion. Each ovary was enlarged to a size corresponding to that of the uterine corpus, and was freely movable and nontender. On Dec. 5, 1935, transuterine pneumoroentgenography and lipiodol instillation revealed the findings indicated in Fig. 1, namely, a small uterine corpus and bilaterally enlarged ovaries. The laboratory findings were negative, and the basal metabolic rate was normal. Surgical intervention was advised, which the patient refused. She subsequently consulted six other gynecologists, and

*Presented at a meeting of the Chicago Gynecological Society, October 18, 1940.

received prolonged treatments with a variety of hormones including equine gonadogens, chorionic gonadotropic hormones, estrogens, and progesterones. Only one of the six advised laparotomy. Slight uterine spotting followed some of the glandular therapy. On Sept. 25, 1939, the patient returned and requested surgical treatment, having had *amenorrhea now for almost seven years and sterility for five years.* The findings on bimanual examination were the same as noted on the initial visit.

On Sept. 27, 1939, laparotomy was performed. The uterus was found to be hypoplastic, regular, firm, and freely movable. Both tubes were normal. Each ovary was enlarged symmetrically to the size of the uterine corpus. The tunica albuginea of each ovary was extremely thick and its surface studded with multiple follicle cysts. About two-thirds of each ovary were removed by wedge-shaped resection, and after puncturing the remaining visible cysts, the ovary was closed with fine catgut. Appendectomy was also performed for "mechanical" reasons. The patient left the hospital in ten days, after an uneventful convalescence. The microscopic report of the pathologist (Dr. Otto Saphir) was "multiple simple cysts and fibrosis of the ovary."

The first menstruation occurred on Oct. 21, 1939, or twenty-four days after the operation, and lasted seven days, with moderate flow. Bimanual examination after this period revealed a normal genital status. Menstruation occurred regularly every twenty-eight to thirty-one days thereafter, and the patient conceived after the period of April 25, 1940, having used no contraception for three months. At this writing (October, 1940) she is pregnant approximately thirty-two weeks.

Multiple follicle cysts, crowding the ovarian cortex and causing bilateral ovarian enlargement is not an infrequent cause of amenorrhea and sterility. These symptoms may be explained by an absence of ovulation due to the mechanical "blockade" by the multiple cysts which crowd the surface. Pneumoroentgenography has been a very important adjunct in the diagnosis of bilateral polycystic ovaries, since it is not infrequently difficult or impossible to evaluate the true size of one or both ovaries on bimanual examination. Rectal examination required in virgins rarely reveals the ovarian swellings.

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MEIGS' SYNDROME

Fibroma of the Ovary With Ascites and Hydrothorax

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Fibroma of the ovary associated with ascites and hydrothorax was first called to the attention of the medical profession by Meigs and Cass[1] in 1937. At that time they were able to collect 7 cases. In 1939, Meigs[2] brought the literature up to date with an additional 8 cases. Bomze and Kirshbaum[3] have added two cases since the appearance of Meigs last publication. The importance of accurate diagnosis of this benign neoplasm is obvious when it is noted that of the 17 cases in the literature 15 patients were treated by surgical removal of the tumor and survived. One of the remaining 2 patients was not given the benefit of a laparotomy, and died as a result of the syndrome. The other reported by Bomze and Kirshbaum presented numerous complicating factors and died two days following laparotomy. These authors considered 3 possible mechanisms as the cause of death. First, the presence of a large ovarian tumor interfering with the progress of gestation and causing abortion, combined with the effects of toxemia and exploratory laparotomy. Second, acute glomerulonephritis which was observed on microscopic examination of necropsy material, and third, death as a result of an untreated Meigs' syndrome.

Clinically, the condition may closely simulate advanced pelvic malignancy with peritoneal, and pleural or pulmonary metastases. Cachexia is not uncommon. The patient usually has known of the presence of an abdominal mass for a long time prior to consulting a physician. The ascitic fluid may be so marked that the patient is incapacitated, and the abdominal mass obscured by the distended abdomen. Attention is called to the co-existing hydrothorax by dyspnea which may have been present for months. Sufficient fluid is usually present to give ample physical findings. The diagnosis of Meigs' syndrome is relatively simple if the condition is considered.

The rarity of this condition has prompted us to report a case which has recently come under our observation, and in which the diagnosis was made preoperatively.

V. V., aged 31 years, colored, was admitted to the Charity Hospital March 31, 1940, complaining that her stomach was swollen. Two weeks prior to admission, she began to have generalized cramping pains in her abdomen, which became progressively worse during an interval of approximately six hours. The pains subsided somewhat, and she noticed that her abdomen had become greatly distended. She had no nausea or vomiting. She ate dinner as usual, but the ingestion of food caused a recurrence of the pains. There was little or no increase in the size of the patient's abdomen from the acute onset until admission to the hospital. She had more or less constant cramping pains of varying intensity during the two-week interval. Her bowel function had been unchanged, and no nausea or vomiting occurred at any time.

She had noticed a lumpy mass in the lower abdomen for a year. She had dyspnea on climbing steps for the year prior to admission, which had become progressively more severe and was noticeable on slight exertion during the past month. Occasional palpitation was present, associated with the periods of dyspnea.

She was not confined to bed during the two weeks of her illness, but experienced discomfort on walking. She had no swelling of her feet, ankles, or hands.

The patient had a slight productive cough for one month. There were no hemoptysis, night sweats or chest pain.

Menstrual and Marital History.—The patient reached menarche at 12 years of age. Her periods occurred at a twenty-eight-day interval, lasting five to six days throughout her menstrual life. There was no dysmenorrhea. Her last menstrual period began Feb. 17, 1940. The present menstrual period began March 12, 1940. One pregnancy occurred terminating in a normal full-term delivery when the patient was 13 years of age.

History.—The past and family history revealed nothing of significance.

Physical Examination.—She was a slightly undernourished colored female with a tense protuberant abdomen. Flatness and impaired breath sounds were noted over the right base posterior and lateral to the level of the seventh rib. No râles were noted. Tactile fremites were absent. No abnormalities were noted on examination of the left hemithorax. The heart was within normal limits on percussion and no auscultatory abnormalities were noted. Her blood pressure was 104/78.

Marked symmetrical enlargement of the patient's abdomen was present. The skin was tense. No enlarged veins were noted. A tympanitic percussion note was present in superior portion of abdomen. Dullness to flatness was noted in dependent portions of the abdomen. Shifting dullness and fluid waves were demonstrable. When the patient was in the supine position, a ballotable mass was present in the lower abdomen that extended up to the umbilicus. The mass was very hard and nodular on palpation. The mass shifted from one side of the abdomen to the other as the patient was turned from side to side. The liver and spleen were not palpable. No sacral edema was present.

Genital examination revealed a multiparous introitus with a slight cystocele and rectocele. Bartholin's glands were not palpable. No exudate could be expressed from Skene's glands. The cervix was normal in size and color. A healed laceration was present on the right side. The external os was slightly dilated; the cervix was a little softer than normal in consistency. The uterus was enlarged to the size of an eight weeks' pregnancy with a single fibroid palpable

on the anterosuperior surface. The fibroid was approximately 4 cm. in diameter. The uterus was anteflexed and freely movable. The mass present in the lower abdomen extended into the pelvis, was freely movable, and was discrete from the uterus; it was noted on the left side. Slight fixation of the right adnexa was noted.

The extremities presented no gross abnormalities. No pitting edema was present.

Laboratory examination revealed no abnormalities.

Diagnosis.—Fibroma of the left ovary and uterine fibroids associated with ascites and hydrothorax.

X-ray examination of the chest on March 16, 1940, showed increased density in lower third of right hemithorax with slight displacement of the heart to the opposite side. Diagnosis: Fluid in the right pleural cavity.

Laparotomy on March 21, 1940, revealed a large solid tumor of the left ovary approximately 12 cm. in diameter. It was very hard and glary white in appearance. The surface was irregular. A long pedicle was present. Approximately four liters of clear fluid escaped from the abdomen when the peritoneum was opened. Uterine fibroids, chronic inflammatory disease of the right tube and ovary, and chronic appendicitis were also present. A total hysterectomy, bilateral salpingo-oophorectomy and appendectomy were done.

The pathologic report showed a large tumor mass of the left ovary, 14 cm. in diameter, slightly lobulated and very firm in consistency. On cut section the surface was yellowish white in color and contained a cystic portion 3 cm. in diameter. The tumor was largely covered by peritoneum and several dilated vessels were noted on its outer surface.

The uterus and cervix measured 10 by 9 by 3.5 cm. The cervix was lacerated unilaterally. The mucosa was smooth and pale yellow. A subserosal tumor mass was present which measured 3 cm. in diameter, well encapsulated, and firm in consistency. The endometrium measured 3 cm. in thickness and was pale yellow and soft in consistency. The right ovary was adherent to the tube and the fimbriated end was closed. The ovary contained a cyst filled with hemorrhagic fluid, other cysts present contained clear yellow fluid.

Final Microscopic Diagnosis.—Fibroma of the ovary, leiomyoma of the uterus, follicular cysts of the ovary, chronic salpingitis, and chronic appendicitis.

The patient's convalescence was particularly uneventful, and she left the hospital April 3, 1940. The patient was entirely free of symptoms during her convalescence

X-ray examination of the chest on April 1, 1940, the 12th postoperative day, showed clearing of the opacity previously seen in the lower portion of the right chest.

Follow-Up Examination.—The patient was seen on Sept. 19, 1940. She had been entirely well since operation, had gained weight and had been able to resume her full duties about the household.

This patient presents the classical Meigs' syndrome. We agree with Meigs' recommendation that paracentesis, be done, if necessary, for accurate diagnosis of the pelvic mass. However, when paracentesis and thoracentesis are done, rapid reaccumulation of the fluid occurs. There is the danger of secondary infection of the affected serous cavities, which occurred in one of the reported cases. We were fortunate that the fibroma of the left ovary was readily palpable in spite of a relatively massive ascites and that the patient was not sufficiently embarrassed by the pleural transudate to require its removal.

There is little doubt that many cases of Meigs' syndrome have been overlooked in the past.

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FULMINATING SYSTEMIC HEMOLYSIS FOLLOWING INCOMPATIBLE BLOOD TRANSFUSION

Use of Sodium Bicarbonate Infusion in Therapeutic Management, With Recovery

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ALKALINE medication as an addition to therapeutic management of blood transfusion complications has its strong advocates since the experimental work of DeGowin on hemoglobin precipitation in acid tubular urine. In accordance with these views, a case of generalized fulminating hemolysis due to incompatible blood transfusion is being reported with the use of sodium bicarbonate intravenously as the basis of treatment. This was instituted less than two hours after hemorrhages from skin, buccal mucous membranes, gingival margins and the gastrointestinal tract were noted. That a similar condition had developed in the genitourinary tract was also revealed by bladder catheterization some hours later.

It is the consensus of opinion that among the serious complications involved in blood transfusion reactions, whether due to compatibility or incompatibility of blood, those relating to the kidneys are unusually severe. The suppression of urine in this case parallels that reported by others with the noticeable difference that it was of shorter duration. Since there has been such scant mention of alkaline medication in other published reports of blood transfusion anuria and treatment, the adoption of sodium bicarbonate here with the relatively early return of renal function merits consideration as a valuable agent therapeutically.

Another incidental fact in this case is also worthy of mention. This has to do with the surgical procedure and the subsequent choice of anesthesia. Because of persistent uterine bleeding as the result of incomplete criminal abortion, curettage was necessary. A spasm of the cervix prevented sponge forceps removal of the retained secundines, and spinal anesthesia was selected. As far as is known, this is the first instance that a spinal type of narcosis was used under such circumstances.

Mrs. E. B., aged 25 years, was admitted to the Jersey City Medical Center with a history of having attempted abortion by instrumentation self-performed. She had previously had three full-term pregnancies and four induced abortions. Prior to admission she stated that she had felt quite chilly on several occasions and noticed the passage of a number of clots from the vagina. When first seen at the hospital, her temperature was 103.8° F.; pulse, 104; respirations, 26. The red blood cell count was 2,970,000; hemoglobin, 40 per cent; white blood cell count, 9,780.

The following day she was taken to the operating room for a transfusion by the direct method. A little more than 200 c.c. of blood had been given when, without any warning, the patient went into sudden shock. Her face became cyanotic and she began to gasp for breath. Beads of perspiration appeared over her entire countenance, and she started to develop chills and shake so severely that she almost threw herself off the operating table. Complete vascular collapse occurred and the pulse was unobtainable.

The transfusion was immediately discontinued and the patient placed in Trendelenburg position and wrapped in blankets. With the transfusion needle still in situ, 2 minims of adrenalin, 1:1000 solution, were introduced into the circulation, and 200 c.c. of 5 per cent glucose in saline injected. The collapse then improved sufficiently for her to be removed to the ward. Here she was given oxygen continuously by nasal catheter and the glucose infusion was continued.

Shortly afterwards she developed fairly profuse vaginal bleeding which required packing, since any other manipulation directed toward removal of the uterine contents was considered too hazardous at this time. Numerous areas of purpura were noted about the body and bleeding had begun to develop at the gingival margins. In the meantime a recheck of the blood grouping was done, and it was discovered

that through an error the name of an incompatible donor had been sent. The patient was Type 2, Jansky, and the donor was found to be Type 3, Jansky.

It was at this point that the administration of sodium bicarbonate, within two hours after the reaction, was begun. Fifty cubic centimeters of a 2 per cent solution were used and repeated every four hours until the urine showed alkaline, once the anuria, which subsequently developed, had been overcome.

On catheterization twelve hours after the transfusion, a total of 50 c.c. of bloody urine was obtained. At this point the patient was becoming very restless, complained of lumbar pains, and showed slight puffiness of both eyelids. The bleeding of the gums was becoming more evident and the vaginal bleeding more profuse.

The following morning, since the uterine hemorrhage persisted, the patient was taken to the operating room for sterile vaginal inspection. On examination a steady stream of blood was seen to be issuing from the cervix. The fluid had no clotting tendency, and it was found necessary to dilate the cervix and remove the remainder of the conception product. The patient was given 50 mg. of novocaine in the spinal canal and the procedure quickly carried out. The entire uterine cavity was firmly packed after the removal of the retained placenta.

The need for blood replacement was evident, and she was given 500 c.c. of blood from a Type 2, Jansky, compatible donor without any reaction. About four hours later the patient had an emesis of about 100 c.c. gastric contents which were dark brown in color and gave a positive test for blood. The vaginal hemorrhage continued slight in spite of the firm packing for almost twenty-four hours and then stopped almost spontaneously.

During the next twenty-four hours, or two days following the incompatible transfusion, the urinary output was 6 c.c. On the third day, the patient vomited about 200 c.c. of fluid, still dark brown in color, and complained of weakness throughout her entire system. She could scarcely lift her head. At this stage, since there was no urinary output, she was given hot, moist packs every three hours in an effort to promote diaphoresis. Symptomatically, she also felt better after these treatments.

On the fourth day she was able to sip small amounts of tea and retain it, and she, generally, showed more interest in herself. Her first voluntarily voided urine appeared on this day. It was exactly 30 c.c. and was reddish in color. The next day she voided 182 c.c. but complained of a tired feeling. She was somewhat nauseated on taking fluids and these were discontinued. Jaundice was very marked by now, although it had begun to appear on the second day. The lumbar pains were very severe at this time. It was significant that on this day, the fifth since the introduction of the incompatible blood, the urine first showed alkaline reaction.

From then on there was daily renal excretion. The sixth day, it was 148 c.c. and increased gradually thereafter. Coincidentally with the kidney output, her symptoms showed steady improvement. Amounts of urine passed later were 450 c.c. on the tenth day; 1,475 c.c. on the eighteenth day; 2,000 c.c. on the nineteenth day; and 2,900 c.c. on the twentieth day.

The nonprotein nitrogen values reached high figures at times. On the day after the original transfusion, the nonprotein nitrogen reading was 62 mg./100 c.c. of blood. Four days later it had reached 103 and at one time was as high as 190 mg./100 c.c. of blood. The icteric index was 61 on the second day and finally came down to within normal limits within two weeks. The patient was discharged after thirty-eight days in the hospital, feeling perfect in health and presenting no complaints.

DERMOID CYST OF THE OVARY WITH SQUAMOUS CELL CARCINOMA

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DERMOID cysts of the ovary are, as a rule, benign in character. Malignant degeneration in a dermoid cyst is infrequent. According to Lynch and Maxwell,[1] carcinoma may develop in an ovarian dermoid in three ways: (1) By direct extension from a carcinoma of an adjacent organ, or by metastasis from a more distant one. (2) By extension from a carcinoma, primary or metastatic, which has developed in the ovarian tissue not concerned with the dermoid growth. (3) By malignant degeneration of the epithelial structure of the dermoid itself. Carcinoma arising in the epithelial structure of the dermoid itself is a rather rare condition. Masson and Ochsenhirt[2] in a review of all cases reported up to 1929 considered only 33 to be proved cases of primary epithelioma of the epithelial elements of dermoid cysts. Some of the reported cases were rejected by them because of the too meager microscopic description of the specimens; some because of the failure on the part of the author to state definitely the origin of the carcinoma. Others were rejected because they were frankly not cases of carcinoma. To these 33 cases, Masson and Ochsenhirt added 4 more. In 1934, Counseller and Wellbrock[3] reported 3 additional cases, making a total of 7 cases out of 408 dermoid cysts surgically removed at the Mayo Clinic from 1912 to 1931, or 1.7 per cent. This figure corresponds with that arrived at by R. Meyer in a collective review of 1,268 dermoid cysts as quoted by Novak.[4]

It is because of the comparative rarity of this condition that the following case is considered worth reporting.

R. F., 38-year-old white female, was admitted to the Beth Moses Hospital Aug. 29, 1940, on the service of Dr. Aaron Hirsch, complaining of pain in the lower abdomen for the past two months, and acute urinary retention four days prior to admission. For the last two weeks pain became more severe and localized in the right lower quadrant of the abdomen. Four days ago, the patient had an attack of urinary retention which lasted for twenty-four hours and required catheterization. Patient noted that the size of her abdomen increased within the last few weeks.

Menses started at the age of 11 years, occurring every thirty-one days, lasting two days at a time without any pain. Her last menstrual period started on Aug. 23, 1940, and was normal in time and duration. Patient had one normal pregnancy ten years ago. There was no history of miscarriages or abortions.

Abdominal examination revealed the presence of a hard irregular mass arising from the pelvis, filling the entire hypogastrium and right iliac fossa. The mass was slightly movable and not tender. Vaginal examination showed a multiparous outlet. The cervix was felt high under the symphysis pubis. There was a hard irregular mass incarcerated in the pelvis and extending upward into the abdomen. The adnexa could not be palpated independently of the mass. A diagnosis of multiple fibroids of the uterus was made and an operation was advised.

Her blood pressure was 112/74. The hemoglobin was 12 Gm. per 100 c.c., red blood cells 5,000,000, white blood cells 14,300 per c.mm. of blood, with 88 per cent polymorphonuclear cells and 12 per cent lymphocytes. Blood sugar 75 mg., urea nitrogen 11 mg. per 100 c.c. of blood. Urine examination was essentially negative.

On Aug. 31, 1940, a laparotomy was performed under cyclopropane anesthesia, and the following was found: The uterus was situated anteriorly and to the left, slightly enlarged, containing two small fibroids on the fundus. Posterior to the uterus and filling the entire cul-de-sac was an ovarian cyst the size of a fetal head. It was firmly adherent to the posterior layer of the broad ligament, pelvic floor, and posterior surface of the uterus. Left adnexa was normal. A right salpingo-

oophorectomy was performed. The cyst was lifted out of the pelvis with great difficulty due to the dense adhesions. During this procedure the tumor was opened and found to be a dermoid cyst. The two small fibroids were enucleated.

The pathologic description of the specimen by Dr. A. Kantrowitz follows:

Gross.—Specimen consisted of two pea-sized firm, pearly-gray masses of tissue which on cross section present the characteristic appearance of fibromyomas; and a mass, the contents of which have been emptied. The measurements of the mass could no longer be determined, although it appeared to have been about the size of a grapefruit. This cystic mass was filled with hair and sebaceous material. The wall measured up to 0.2 cm. in thickness, but in one area, 7 cm. in diameter, the wall measured up to 2 cm. in thickness. In the thickened area, the wall presented a mottled grayish yellow color and a rather firm consistency. The serosa of the cyst was entirely smooth except over the thickened area, where a number of umbilicated areas were noted with considerable roughening of the serosa. A small portion of the tube, with fimbriated end, was attached to the specimen. This portion measured 3 cm. in length. Another portion of tube, measuring 4.5 cm. in length, was received separately.

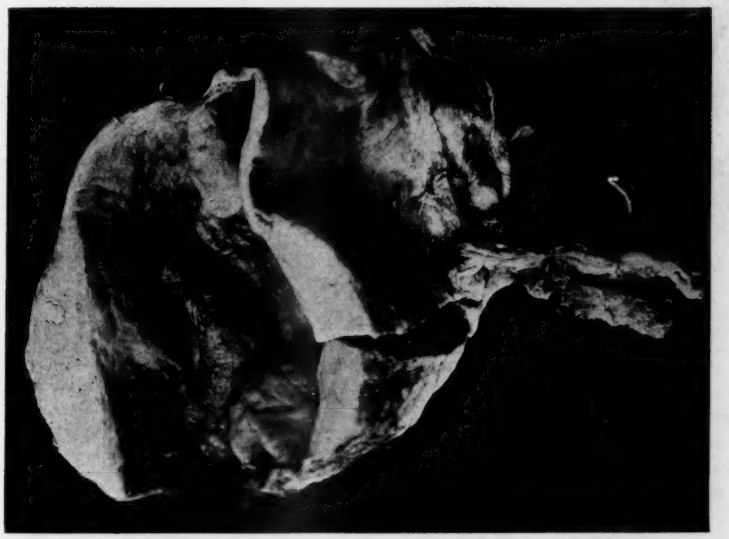

Fig. 1.—Gross specimen, showing thin cyst wall with edges of the thickened area, the seat of the carcinoma, in the foreground.

Microscopic.—The cyst wall was lined by stratified squamous epithelium. The thickened area contained nests and intercommunicating strands of polyhedral, flattened cells with a clear to granular basophilic cytoplasm. The nuclei vary considerably in size, shape, and staining capacity. Mitotic figures were noted frequently. The greater portion of the thickened mass was necrotic. Areas of normal ovarian tissue were also invaded by the epithelial cell nests. The roughened surface areas were also invaded, showing nests of epithelium on the denuded areas. The inner surface of the mass showed a complete denudation of its epithelium. The tube showed no changes. The small masses consisted of smooth muscle bundles in a connective tissue stroma.

Diagnosis.—Epidermoid carcinoma in a dermoid cyst of the ovary (right); small fibromyomas.

The postoperative course was complicated by vomiting which became severe on the sixth day after operation. There was no abdominal distention. Inspection of the wound showed normal healing. A Miller-Abbott tube was passed and retained for seven days. The patient stopped vomiting, and had normal bowel movements.

The tube was removed on the fourteenth day postoperative. The patient left the Hospital one week later in good condition.

This case is obviously one of primary epithelioma in a dermoid cyst arising from the epithelial elements of the tumor. While the condition is rare, it is well to bear the possibility of its presence in mind, especially if the tumor is adherent or gives unusual pressure symptoms. Careful microscopic study of each dermoid cyst is imperative. Prompt surgical removal of an ovarian tumor diagnosed as a dermoid cyst would seem advisable.

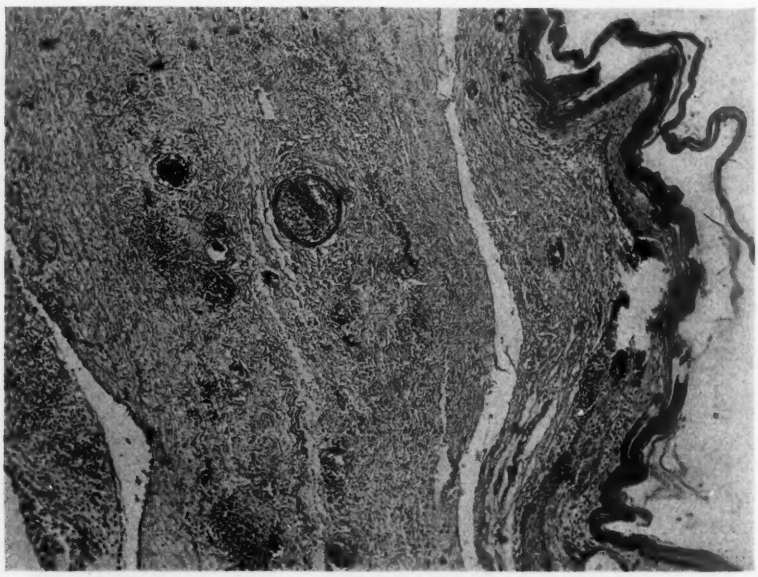

Fig. 2.—Photomicrograph of cyst wall, showing lining of stratified squamous epithelium.

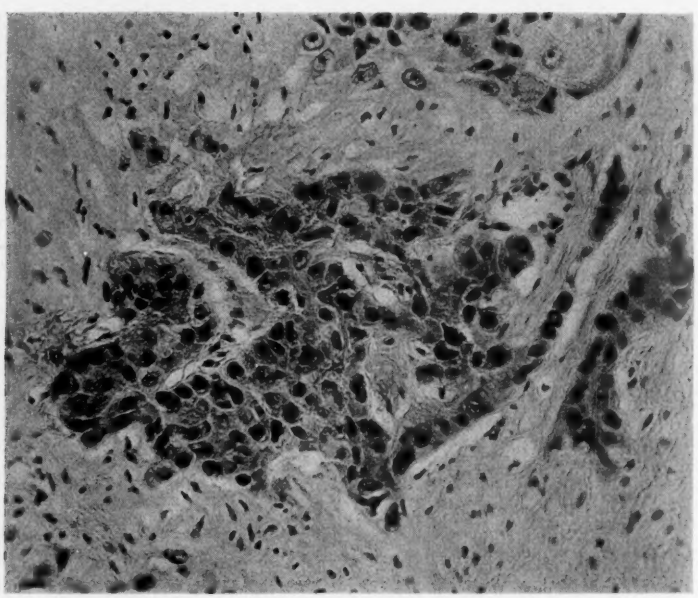

Fig. 3.—Photomicrograph showing epithelial cell nest invading thickened area; nuclei vary in size, shape, and staining capacity; mitotic figures are present.

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HERPES GESTATIONIS

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HERPES GESTATIONIS is a rare cutaneous complication of pregnancy characterized by a multiform, vesiculobullous dermatitis, marked by severe burning and itching, and affecting primarily the trunk, legs, forearms, and face. The exact etiology is unknown. It is thought by many that the cutaneous lesions result from injury to the vasomotor nerves by toxins produced by ferments from fetal tissues, or by cells from chorionic villi. It pursues a chronic course, starting usually during the latter half of gestation and ending within a few weeks after delivery. Occasionally, the condition may occur in the puerperium. It is pointed out that in these cases the eruption may result from retained placental tags. This complication tends to recur with subsequent pregnancies.

Ormsby[1] defines herpes gestationis as a variety of dermatitis herpetiformis occurring in pregnant women. According to Riecke[2] whose review of the subject is the most complete, Bunel[3] was the first to describe this condition in 1811. Since then, this rare dermatitis was described under many terms such as pemphigus pruriginosus, herpes circinatus bullosus, dermatitis multiformis gestationis, etc. The term herpes gestationis was first used by Milton[4] in 1872 and is at present the universally accepted term for this cutaneous complication of pregnancy.

That herpes gestationis is a rare occurrence can be seen from the statement of Irving[5] that no patients with this dermatosis have been admitted to the Boston Lying-in Hospital during the past twenty years. Many obstetricians (personal communications) have never encountered this disease. In the past ten years only 6 case reports of herpes gestationis have appeared in the American literature.[6-9] Hence, the report of an additional classical case is justified.

An Italian woman, aged 32, para i and gravida ii, presented herself to the prenatal clinic on Aug. 26, 1939, with a complaint of amenorrhea since June 19, 1939. Her personal and family history did not disclose any significant facts, except that her first pregnancy in 1936 was complicated by a skin eruption which appeared during her fifth month of gestation and cleared up several weeks after a spontaneous delivery at term of a seven and one-half pound living and healthy male infant.

Examination revealed that the uterus was enlarged to the size of a two months' pregnancy. Her pelvis was adequate and at this time there was no evidence of any skin or mucous membrane lesions. The heart, lungs, abdomen, ear, nose, throat, and extremities revealed no pathologic findings. There was a slight trace of albumin in the urine, a negative blood Wassermann and Kahn reaction, and a blood count within normal limits.

She returned on Nov. 18, 1939, in her fifth month of gestation complaining of attacks of intense itching and a skin rash. At this time examination revealed a discrete vesiculo-bullous eruption on her abdomen, chest, and both ankles. The eruption consisted of large patches or plaques roughly annular, clearing in the center and progressing on the periphery. As the older lesions involuted new lesions in the form of vesicles and bullae would appear. There were periods varying from a day to ten days during which time the patient was free of attacks of itching and of new lesions. There were no lesions on the mucous membranes.

Her temperature was normal. The blood count disclosed 11,850 leucocytes, 59 per cent polymorphonuclear neutrophiles, 16 per cent lymphocytes, 15 per cent eosinophiles, 3 per cent monocytes, and 7 per cent stems. Examination of the stools did not disclose any evidence of parasites to account for the eosinophilia. At this time a diagnosis of herpes gestationis was made.

She was advised to take potassium permanganate tub baths, to use a drying lotion, and Fowler's solution (Liq. potass. arsenitis) was ordered in ascending doses beginning with one drop and increasing one drop daily. She reported to the dispensary each week. Fresh bullous efflorescences continued to appear even when the patient was taking seven drops of Fowler's three times a day. Fowler's solution was therefore discontinued and an effort was made to treat her with injections of serum taken from the blood of normal pregnant women. Two to 5 c.c. of the serum was injected intramuscularly twice a week for three weeks without any visible improvement in her condition.

Fig. 1.—Showing the distribution of the eruption during the fifth month of pregnancy.

On Feb. 12, 1940, the patient was hospitalized. On admission to the hospital her general condition was fair. There was a slight rise of temperature. The eruption by now was generalized, covering the face, extremities, chest, back, and abdomen. The bullous type of lesion predominated. Her blood pressure was 126/70. There was no evidence of any visceral pathology. Laboratory examinations disclosed the following findings: The urine was acid and contained traces of albumin. The blood showed 4,900,000 erythrocytes, 95 per cent hemoglobin, 18,200 leucocytes, 74 per cent polymorphonuclears, 3 per cent eosinophiles, 19 per cent small lymphocytes, and 4 per cent monocytes. A gastric analysis revealed a total HCl of 40 and a combined HCl of 4. The blood chemistry findings were as follows: Sugar 69 mg., calcium 8.8, urea nitrogen 12.6, nonprotein nitrogen 24, creatinine 1.42, cholesterol 238.

It was felt that perhaps a hormone disturbance may be responsible for this disease, hence we decided to use estrogen therapy. From Feb. 12 to 18, 1940, the patient received 600,000 units of progynon B, and 70 mg. of proluton, without any influence on the eruption. Forty grains of sulfanilimide daily were tried for eleven days, and 40 gr. of sulfapyridine daily were used for six days without any amelioration of the signs or symptoms of the disease.

The patients general condition became worse. There were numerous new crops of bullae, the itching was intense, and she appeared very uncomfortable and toxic. A medical induction was therefore decided upon. On March 2, 1940, at 10 A.M., twenty-four days before the calculated date of delivery, 1½ ounces of castor oil and 9 gr. of quinine were administered. Uterine contractions started several hours later, and on March 3 she delivered spontaneously a six-pound living male. On the thirteenth post-partum day she still had some bullae although new bullae ceased to appear four days post partum. Six weeks post partum all her skin lesions cleared, leaving only hyperpigmented patches. The baby was in good condition.

SUMMARY

A case of recurrent herpes gestationis, an exanthematous manifestation of a toxemia of pregnancy, is reported. Efforts to modify the course of the disease by the use of hormonal (estrogenic and corpus luteum) and chemotherapeutic (sulfanilamide and sulfapyridine) measures have failed.

We are indebted to the Schering Corporation for the supply of progynon B and proluton.

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DIABETES INSIPIDUS COMPLICATING PREGNANCY

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CASES of diabetes insipidus manifesting themselves as such only during the period of gestation and absent during the intervals between pregnancies are extremely rare. The case to be reported here is one in which the diabetes insipidus made its appearance about the sixth month of the pregnancy and ended abruptly on the seventh post-partum day. To the present time the patient has been seen at various intervals, and there is no evidence of any return of the symptoms. She has not become pregnant again due to voluntary sterility.

Mrs. H. B. C., aged 22 years, primigravida, was first seen on Sept. 23, 1933. Her last menstrual period started July 23, 1933, making her due April 30, 1934. Her past history was essentially negative as was her menstrual history.

Physical examination revealed a rather tall thin, asthenic type of female with no striking physical abnormalities. Her weight was 115½ pounds and blood pressure 110/70. Pelvic examination was negative except for the uterus which was soft, and symmetrically enlarged to about the size of a six weeks' pregnancy. The pelvis appeared to be ample.

The patient had a minimal amount of nausea, but otherwise progressed normally until the first week of her sixth month, when she noticed that she had to drink large quantities of water and was passing large amounts of urine. The patient was asked to measure her intake and output and she reported that it varied from twelve to sixteen quarts of water per day, with a corresponding output of urine.

Urinalysis at this time revealed nothing except a decrease in the specific gravity. Blood sugar, Wassermann test, and stereoroentgenograms of the sella tursica were all normal.

The patient was treated with 50 mg. of posterior pituitary powder by nasal insufflation q.i.d. This caused a rather marked reduction in symptoms to a point

where the patient only had to take three to six quarts per day. Her urinary output decreased in proportion. The patient tolerated this amount very well, but when an attempt was made to increase the dosage she developed a rather marked rhinitis. There was ever present the possibility that the posterior pituitary extract might stimulate uterine contractions and thereby cause the delivery of a premature infant.

The patient continued in this manner until April 4, 1934, when after a normal labor, she spontaneously delivered an eight-pound, living male infant.

During the first six days of her puerperium her intake remained at about six to seven quarts per day. On the seventh post-partum day, her intake abruptly dropped to one quart and has remained within normal limits ever since.

DISCUSSION

The exact etiology of diabetes insipidus is at the present time not clearly understood. It has been ascribed by some workers to be purely a deficiency in posterior pituitary lobe secretion. This is somewhat borne out by the excellent clinical results often obtained by the administration of posterior lobe extract.

Others believe that normally there is an antagonistic relationship between a diuretic hormone of the anterior pituitary, and an antidiuretic hormone of the posterior pituitary, and that occasionally this may become disrupted with a resulting relative increase in anterior lobe secretion. To support this view they offer the evidence that in the cases reported, the condition ceased abruptly in the early days of the puerperium, and this is about the time that the Aschheim-Zondek reaction became negative and signified a decrease in the amount of anterior lobe secretion.

Experimentally, it has been possible to reproduce the condition by injuries to the hypothalamus or to the nervous connection between the pituitary and the hypothalamus.

In the light of the present knowledge, it is probably more correct to look upon the condition occurring as the result of a disorder affecting the pituitary-hypothalamic mechanism and its nervous connection rather than being specifically dependent upon either the pituitary or hypothalamus alone.

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1911 Wilshire Boulevard

Madilhac, P.: Evipan as a General Anesthetic in Gynecology, Presse méd. 48: 252, 1940.

For anesthesia of short duration evipan is valuable as it is easily handled without danger to the patient.

As a prolonged general anesthetic evipan carries no more danger than any other general anesthetic. The author reports 1.8 per cent abnormal reactions but fails to mention the number of cases in his series. The technique is easy and utilizes minimal apparatus. Evipan induces an unusually quiet abdomen which in gynecology is an asset.

The insensible and painless induction is particularly appreciated by the nervous patients. The chief advantage of evipan over other anesthetics is the rarety of postoperative pulmonary complications following its use. The drug should be administered by an experienced anesthetist.

Clair E. Folsome.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

A STUDY OF PUERPERAL MORTALITY IN NEW YORK CITY (1937-1940) WITH ESPECIAL REFERENCE TO PREVENTIVE FACTORS*

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IN 1937 the New York County Medical Society appointed a Maternal Welfare Committee to study all puerperal deaths occurring in the Borough of Manhattan. Meetings open to all members and held at monthly intervals when the records of puerperal deaths are presented in detail. Anonymity of patient, doctor, and hospital is maintained. This tends to promote a more frank discussion than would be possible otherwise and greatly increases the educational aspects of the meetings.

Our knowledge concerning the statistical aspects of puerperal mortality has been fairly reliable during the present century. In general, however, the information acquired at the present time is more detailed and accurate than that previously compiled. It is to be hoped that future trends based on these comprehensive data will make more pleasant reading than some of the reports submitted in the past.

The average "puerperal mortality" rate in New York City for the first 35 years of the present century was approximately 52 per 10,000 reported terminated pregnancies. In the four years following (1936 to 1939), the rates were 44.3, 38.2, 33.4 and 29.6, respectively. Undoubtedly, then, the rate dropped rather abruptly beginning with 1936, while previous to that year there was no significant trend in either direction There is no correlation between the birth and the puerperal mortality rates as the former has decreased progressively from approximately 36 to 14.5 per 1,000 population while the latter remained essentially the same during the thirty-five years referred to. The birth rate has been relatively stable during the past few years when the significant decrease in the puerperal rate occurred. There has been an almost comparable decrease in the puerperal mortality as revealed by our national figures so that the factors responsible for the improvement are probably largely national rather than local in scope. One can only speculate on the effect of certain known local conditions, such as, improved diet and housing made available by relief to the lower economic classes, earlier and better prenatal care to the same group, increased medical interest in and study of the problem in general, better education of medical students in the theory and practice of obstetrics, and the educational effect of the various maternal welfare groups appointed by the county medical societies, in promoting the practice of better obstetrics.

A careful interpretation of a statistical analysis by Duffield[1] of puerperal deaths occurring in New York during the year 1939 reveals the following important facts:

1. The puerperal mortality is much higher in the colored as compared to the white race, and the rate increases progressively with advancing age, irrespective of parity (Table I). The death rate in city hospitals exceeds that of voluntary hospitals by approximately two and one-half times.

2. If we compare the 1939 rate with the average of the 1931 to 1935 rates, it becomes evident that deaths ascribed to abortion, toxemia, and "all other" causes have decreased in excess of the average decrease in all causes, while the percentage of deaths associated with infection and hemorrhage has diminished relatively little (Table II). In fact, nearly one-quarter of all puerperal deaths in

*Read at a meeting of the New York Obstetrical Society, Oct. 8, 1940.

1939 were caused by infection following premature or term labor and if deaths caused by infection following abortion are included we find that infection was the cause of death in slightly over two-fifths (40 per cent) of all maternal deaths.

TABLE I. COMPARISON OF PUERPERAL AND MATERNAL MORTALITY IN THE WHITE AND COLORED RACE IN NEW YORK, 1939

	TOTAL REPORTED TERMINATED PREGNANCIES	DEATHS	RATE PER 10,000 TERMINATED PREGNANCIES		
			WHITE	COLORED	TOTAL
Puerperal mortality	108,018	320	25.7	75.7	29.6
Maternal mortality	104,684	246	21.2	50.4	23.5

TABLE II. PUERPERAL MORTALITY BY CAUSE IN NEW YORK CITY. RATE PER 10,000 TOTAL BIRTHS

CAUSE OF DEATH	TOTAL	ABORTION	HEMORRHAGE	SEPTICEMIA	TOXEMIA	ACCIDENTS OF CHILDBIRTH (INCL. CESAREAN SECTION)	ALL OTHER
INTERNATIONAL LIST NUMBER	140-150	140-141	144	145	146-147	149	142 143 148 150
Average rate 1931 to 1935	54.4	10.5	6	8.2	7.8	12.6	10
Rate 1939	29.6	4.6	4	6.8	3.4	6.7	4.1
Decrease	24.8	5.9	2	1.4	4.4	5.9	5.9
Per cent decrease	45.6	56.2	33.3	17.1	56.4	46.8	59

3. The incidence of cesarean section is 2.4 per cent; the lowest rate prevails in the municipal (1.6 per cent) and the highest rate in the voluntary hospitals (3 per cent). Sixty-eight, or 2.7 per cent, of the 2,558 patients operated upon (cesarean section) died during or following the operation. The role of this operation as a cause of death would appear significant if the following facts are taken into consideration as revealed in Table III. The type of patient cared for in the different institutions obviously plays an important role.

TABLE III. CESAREAN SECTION, CITY OF NEW YORK, 1939. INCIDENCE, MORTALITY, AND PERCENTAGE OF ALL PUERPERAL DEATHS CORRELATED WITH TYPE OF INSTITUTION

	CITY AS A WHOLE	MUNICIPAL HOSPITALS	VOLUNTARY HOSPITALS	PROPRIETARY HOSPITALS
Incidence of cesarean section	2.4	1.6	3.1	1.9
Mortality in patients delivered by cesarean section	2.7	5.1	2.1	3.3
Per cent of all puerperal deaths associated with the operation	21.3	12.6	26.0	34.2

A more detailed study of important causes of death becomes necessary before constructive suggestions may be advanced. With very few exceptions something constructive should be obtained from every death. All must agree that, with the data available, it is quite improbable that any two individuals could agree entirely on the analysis relative to indication for operation, technique of procedure or other opinion that may be expressed.

Cesarean Section.—Since the inauguration of the Committee of New York County, 58 deaths associated with cesarean section have been studied and are available for analysis at this time. It is understood that some of these deaths are in

no way related to the procedure of delivery involved, on the other hand, certain deaths appear to have been definitely due to the operation.

The indications for operation are listed in Table IV. In many instances multiple

TABLE IV. INDICATIONS FOR CESAREAN SECTION, 58 CASES

Clinical dystocia (after trial labor)		13
Contracted pelvis		10
Clinical diagnosis	5	
X-ray diagnosis	5	
Previous cesarean section		8
Placenta previa		6
Premature separation of the placenta		2
Other		19
Heart disease	4	
Pre-eclampsia	4	
Failed forceps	1	
Myomas	3	
Abnormal presentation	2	
Uterine inertia	1	

indications make it difficult to determine the most important cause. For this and other reasons little discussion appears necessary concerning the indications, excepting to note that 8 cases (one-seventh approximately) were done primarily because of a previous cesarean section. One can realize how the initial maternal mortality associated with this operation does not tell the whole story. The pyramiding effect of maternal mortality becomes apparent where the termination of subsequent pregnancies by this means is done primarily because of the history of a former operation. In general, our experience indicates that close scrutiny of possible contraindications to operation may be equally important to a careful survey of the indications.

Anesthesia was directly responsible for three deaths. A careful study of the individual records leads me to believe that it played an important role in eight additional cases. Table V summarizes the anesthetic agents employed.

TABLE V. TYPE OF ANESTHESIA EMPLOYED IN 58 CASES OF CESAREAN SECTION

Nitrous oxide plus ether	39
Cyclopropane	5
Local	3
Other	3
Unknown	8

I believe that if 90 per cent, instead of 5 per cent, of these operations had been carried out under local anesthesia there would have been a definite reduction in the mortality. The various advantages of local over general anesthesia will be discussed later.

TABLE VI. CAUSE OF DEATH IN CESAREAN SECTION

	NUMBER	PER CENT
Infection	26	44.8
Hemorrhage and shock	11	17.2
Cardiac	5	8.6
Pneumonia	4	6.8
Toxemia	4	6.8
Anesthesia	3	5.1
Other	5	8.6

The causes of death in these patients are detailed in Table VI. A careful study of the individual cases that make up this material suggests that there are controllable

factors in 53 (91.4 per cent) of the deaths that may have modified the outcome in a considerable number of these patients. If we correlate the cause of death with the type of operation, additional information concerning some of the factors involved is revealed. The data are presented in Table VII.

TABLE VII. TYPE OF OPERATION CORRELATED WITH CAUSE OF DEATH

CAUSE OF DEATH	CLASSICAL OPERATION		LOW FLAP OPERATION		OTHER OPERATIONS*		TOTAL
	NO LABOR	LABOR (3-72 HR.)	NO LABOR	LABOR (1-60 HR.)	NO LABOR	LABOR (24-60)	
Infection	4	3		15		2	24
Hemorrhage	3		4	2		2	11
Other	4	2	5	7	1		19
Totals	11	5	9	24	1	4	

*Porro, extraperitoneal, and peritoneal exclusion. (Four insufficient data to classify.)

I regret that I cannot present the total number and type of operations done in the county during the period that the above deaths occurred. It is quite likely, however, that the incidence would not vary significantly from the figures given in Table III.

The evidence suggests that the low flap operation in the absence of labor reduces the incidence of deaths from infection, but the procedure done under these conditions, namely, with a poorly developed lower uterine segment, may be more dangerous from a point of view of hemorrhage. A low flap cesarean section done after fifteen or more hours of labor is a dangerous procedure in my belief.

Another approach to the cause of death reveals the fact that 16 of the 58 patients, approximately 27 per cent, died on the day of operation; 11 were associated with hemorrhage, 3 with the anesthesia, and 2 died from other causes.

Forty-five of the deaths occurred in 21 voluntary or proprietary hospitals and 13 in three city hospitals. This information does not appear to be particularly constructive and no further comment will be made on the subject.

The gross fetal mortality is not available because information concerning neonatal deaths is lacking. There were, however, 9 stillbirths or deadborn which represent a fetal mortality of approximately 16 per cent. If we deduct the fetal mortality associated with premature separation of the placenta and placenta previa, there still remain 6 deaths representing a fetal mortality of over 10 per cent.

After a careful study of the individual records, there appear to be obvious errors in the management of many of these patients. It is probable that many of them could not have been prevented under the circumstances of present-day practice in this city. With some changes in organization, adherence to well-defined principles and concentrated effort, the results should be modified. In Table VIII

TABLE VIII. POSSIBLE ERRORS IN MANAGEMENT OF CESAREAN SECTIONS

Duration of labor too long before operation	12
Anesthesia	11
Procrastination and delay in transfusion	9
Anemia (ante partum) (Hb. per cent was often unreported)	4
Error in technique	8
Inadequate preoperative care of cardiacs	2
Total	46

the common errors are summarized. At times more than one error has been drawn from a given case.

If something concrete can be done to eliminate such factors as have been cited, a definite decrease in the mortality in this group, which represents approximately one-fifth and one-third of the puerperal and maternal mortality, respectively, in this county, may be expected.

Shock and Hemorrhage.—In 1939, not including deaths attributed to cesarean section, approximately one-sixth of the maternal mortality in New York City was attributed to this cause. In an analysis of the first 171 deaths studied by our Committee, as reported by Schneider,[2] approximately one-third of the deaths were ascribed to hemorrhage, when those from abortion and nonpuerperal causes were excluded.

I do not propose to present a statistical résumé of these cases, but rather a few impressions I have gathered from a study of the case records.

Briefly, the problem presented is the prompt control of hemorrhage and the immediate restoration of blood volume. For this latter purpose whole blood is undoubtedly superior to any of the other commonly employed solutions for infusion. However, it has been our experience that delay in transfusion occurs much too frequently with disastrous results. This can be corrected to some extent by having an available donor actually present or the employment of the blood bank when the possibility of hemorrhage may be anticipated. While preparations for transfusion are being made, blood substitutes are frequently necessary. Crystalloid solutions (saline and glucose) have the objection that the effect usually is only temporary, and second, they are useless in secondary shock which is associated with tissue anoxemia, increased capillary permeability, and acidosis. In actual practice their use may be more deleterious than beneficial. Colloid solutions (acacia), although they are better for purposes of restoring blood volume, must be administered slowly and with great care. Fatalities have been ascribed to their employment. Blood plasma on the other hand, has a number of advantages over these solutions for purposes of restoring blood volume.[3-5] Briefly, pooled plasma with negative serologic reactions for syphilis may be stored under refrigerated conditions, for long periods of time and used as an infusion without delay when an emergency arises. Typing and determination of compatibility are not necessary. Reactions are relatively rare and innocuous and massive amounts may be employed, if necessary, without technical difficulties such as would be encountered in the procurement of an equal volume of whole blood from either a donor or blood bank source. Its prompt use following hemorrhage immediately restores blood volume and prevents the development of secondary shock. I am not advising the employment of plasma as a complete substitute for whole blood, but rather for the immediate restoration of blood volume by this means, instead of attempting to do so by the use of crystalloid solutions, as is common practice at the present time, while awaiting preparations for transfusion.

Infection.—We have been informed that slightly over 40 per cent of the puerperal mortality and slightly more than 23 per cent of the maternal mortality in New York City for 1939 was caused by infection. One year ago this month I presented evidence to this Society[6] that the use of the sulfonamide group of drugs available at the time, in all postabortal and puerperal infections, was unjustified. The frequent employment of these preparations as indicated by the records studied at our Maternal Welfare Meetings appears to support the contention. In my opinion, early bacteriologic investigation into the nature of a given infection should constitute, as a general rule, the first step in the management of such patients. Frequently this has not been the case. Sulfonamide drugs may be indicated in serious fulminating infections before a bacteriologic report is available. This procedure should be the exception, however, rather than the rule.

I have been impressed by the data presented at our meetings concerning chemotherapy by several facts. Briefly, these include, inadequate dosage, lack of bacteriologic investigation, discontinuance of the drug because of "minor" toxic symptoms, changing from one drug to another for various reasons, and persistence in the use of the therapy in the absence of any signs of a favorable response.

Anesthesia.—In addition to the complications already cited when discussing cesarean section, there have been a number of other case records reported before our committee where general anesthesia was responsible to a large extent for the fatal outcome. Unfortunately, the total number of deaths caused by anesthesia in New York City are unknown because of lack of information, and it is interesting to note that only two deaths were attributed to this cause in 1939. Schneider,[2] however, reported 6 deaths due to asphyxia associated with anesthesia in his analysis of the first 171 deaths investigated by the New York County Committee. It would

appear that deleterious effects, as a result of general anesthesia, occur much more frequently than is usually thought to be the case. For these reasons a general broadening of the indications for local anesthesia appears indicated and should include such conditions as upper respiratory infections, other medical complications, toxemias, long labors, and when delivery is to be accomplished by cesarean section.

The wider adoption of the local technique would, I believe, save lives, although certain obstetric procedures such as, version and extraction, breaking-up the frank breech, and other intrauterine manipulations, require deep surgical anesthesia.

I have discussed rather briefly in the preceding pages deaths associated with cesarean section, hemorrhage, infection, and anesthesia. I have not called attention to deaths following traumatic obstetric operative procedures in an attempt to effect delivery through the undilated cervix or to patients with antepartum bleeding who were subjected to examination or to treatment without adequate provision for therapeutic procedures or to the employment of incompatible blood for transfusion or to other ill-advised procedures. Our New York County Committee is of the opinion that improvement in obstetric practice has occurred during the past three years. The character of the discussions at our meetings has improved steadily and the inhibitions of the discussor have been largely removed.

SUMMARY

Certain facts pertaining to puerperal mortality in New York City have been presented. It appears that the rate has been decreasing steadily for the past four years while it remained essentially stationary during the preceding thirty-five years. Etiologic or predisposing factors, such as age, race, place and type of delivery, and important causes of death, are reviewed. In addition, statistical data have been presented on some of the principal causes of death in New York County, hemorrhage, infection and deaths associated with cesarean section and anesthesia. While it is admitted there are other important causes of death, an attempt has been made to emphasize the leading factors at the expense of omission of other phase of the problem. The following suggestions appear worthy of consideration.

1. The puerperal risk involved in the care of underprivileged, elderly, or colored patients is several times greater than that of young, white and the better situated economic group of patients. Lethal complications in the former may be sublethal in the latter. For these reasons such patients demand mature judgment and the best possible care at all times.

2. The more general adoption of local or regional block and greater restriction in the employment of general anesthesia.

3. The use of the classical cesarean operation should be limited to patients who are not in labor. The low flap operation is relatively safe during the early hours of labor; however, the dangers increase progressively as labor advances and the use of this procedure after fifteen or more hours of labor is accompanied by an unwarranted risk to the patient.

4. The employment of blood plasma where whole blood is not immediately available and the exclusion of crystalloid solutions is indicated for the immediate restoration of blood volume following hemorrhage to prevent the development of secondary shock.

5. Early recognition of the nature of infections and the prompt use of the appropriate sulfonamide drugs in adequate dosage where indicated.

6. Active participation by general practitioners and specialists in maternal welfare meetings, believing this medium to be the best available and a very satisfactory method of postgraduate instruction.

7. Assumption of the attitude that every obstetric death involves mistakes in judgment or technique and a constructive attempt to profit from the experience.

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PUERPERAL MORTALITY IN THE BOROUGH OF BROOKLYN, CITY OF NEW YORK*

CHARLES A. GORDON, M.D., F.A.C.S., BROOKLYN, N. Y.

THE number of puerperal deaths in the United States has declined sharply since 1933, the first year that figures from the entire country became available for study. In 1938 the national puerperal death rate was the lowest on record, a decline of 30 per cent from 62 per 10,000 live births to 43.5. The rate for 1939 will be still lower.

In New York City the rate has been more than cut in half since 1933, from 61.1 to 29.6 in 1939. In Brooklyn, however, the crude puerperal rate for 1939 was 26, the lowest in the five boroughs, with 110 deaths, while in 1933 there were 284 deaths, a rate of 70, which was considerably higher than the national and city rate that year. It has been shown, however, by Mr. Thomas J. Duffield, Registrar of Records of the Department of Health, City of New York, that the colored population of New York City, which is largest in Manhattan and Brooklyn, is an important statistical factor, since the puerperal death rate of colored women is nearly three times that of white women. And, since the death rate from abortion is nearly seven times as high among colored as white, Brooklyn is passed by Richmond and Manhattan when deaths early in pregnancy are excluded in calculating the maternal mortality rate.

In Brooklyn substantial reductions in all types of puerperal death have been made, but not uniformly. Deaths from hemorrhage, septicemia, and accidents of childbirth, which includes cesarean section, show a relative increase in the last five years.

In 1939 septicemia was charged with the greatest number of puerperal deaths, 31 per cent of the total, or 42 per cent if deaths from septic abortion exclusive of homicide are included. Only those deaths which are so reported by the Office of the Chief Medical Examiner are classified as criminal abortion. There are of course many more in which evidence is lacking. "It was because of 21 such cases, largely among colored women who died in Harlem, that the puerperal death rate in Manhattan was higher than that of Brooklyn."[2] Table I shows the relative increase of septicemia over a five-year period in Brooklyn, and the part played by operative delivery in 1939.

TABLE I. SEPTICEMIA, 1935 TO 1939

(Abortion excluded)

	1935	1936	1937	1938	1939
Puerperal deaths	197	156	158	127	110
Septicemia	49	45	39	37	34
Percentage of total	24.8	28.8	24.7	29	31

1939	Operations:	Associated:
	12 cesarean (peritonitis)	14 long labors
34 deaths	3 forceps	18 early rupture of membranes
	4 version	
	5 induction	7 hemorrhages

If deaths from hemorrhage are combined with those due to accidents of childbirth as largely due to hemorrhage and shock associated with delivery, we find a similar relative increase. Details are shown in Table II.

*Read at a meeting of the New York Obstetrical Society, Oct. 8, 1940.

TABLE II. HEMORRHAGE AND ACCIDENTS OF CHILDBIRTH

	1935	1936	1937	1938	1939
Puerperal deaths	197	156	158	127	110
Hemorrhage	20	25	21	19	13
Accidents of childbirth	44	36	34	33	29
Percentage of total	32.5	39	34.8	41	38.2

In this total of 76 deaths from septicemia, hemorrhage and accidents of childbirth account for 27 deaths of women who had cesarean section; 3 cesarean hysterectomies are included, 2 of which were for rupture of the uterus after failure of breech extraction, and 2 Waters' extraperitoneal sections, 1 after twenty-eight hours of labor with membranes ruptured seventeen hours, in which patient died of hemorrhage during the operation, and the other not in labor with death ascribed to shock. A general anesthetic was administered in 24 cases, local in only 3. The type of operation is of interest.

TABLE III. 110 PUERPERAL DEATHS, 1939; 27 CESAREAN SECTION DEATHS, 24.5 PER CENT

TYPE OF OPERATION	TOTAL	OPERATOR	
		OBSTETRICIAN	OTHER
Classical	15	7	8
Lower segment	7	7	—
Waters	2	2	—
Hysterectomy	3	3	—

To the classical operation is assigned the greatest number of deaths (15). It is noteworthy that intestinal obstruction caused death in 3 of these cases. In 8 women, not in labor, death was due to peritonitis (3) and intestinal obstruction (2), in the other 7 it will be seen that this operation was performed after many hours of labor, with death largely due to peritonitis.

TABLE IV. 15 CLASSICAL CESAREAN DEATHS, 1939*

HR. IN LABOR	HR. MEMBRANES RUPTURED	ANESTHESIA	DEATH
6	0	General	Peritonitis
6	6	General	Peritonitis
14	0	General	Eclampsia
28	0	Spinal	Obstruction
36	0	General	Peritonitis
36	24	General	Peritonitis
47	3	General	Peritonitis

*Eight not in labor. Peritonitis, 3, shock, 3, obstruction, 2; 7 in labor.

The lower segment operation was performed in 7 cases of cesarean section deaths, as shown in Table V.

TABLE V. 7 LOWER SEGMENT CESAREAN DEATHS

	HOURS IN LABOR	HOURS MEMBRANES RUPTURED	ANESTHESIA
Peritonitis	6	17	General
Peritonitis	10	16	Local, General
Peritonitis	15	39	General
Peritonitis	40	0	Local
Embolism	0	2	Local-Gas
Sepsis and embolism	5	6	General
Aspiration	13	8	General

Since cesarean appears as a cause of death in 27 of the 110 cases of puerperal death in 1939, a ratio of 1 to 4, it has seemed wise to present it thus in detail. The Bureau of Vital Statistics has assigned 12 of these deaths to septicemia. It is clear then that reduction in the number of cesarean deaths will lower considerably the number of deaths in this rubric.

Anesthesia in itself is a definite hazard. During the three-year period, 1937 to 1939, anesthesia was the actual cause of death in 13 cases in the entire number of 395 puerperal deaths. If this may be compared with 20 in the 2,041 deaths analyzed in the New York Academy of Medicine report, more than three times as many deaths occurred from anesthesia as might be expected. In 9 of these cases there were definite controllable factors, as the use of ether in toxemia (2), spinal anesthesia for cesarean during cardiac decompensation (1), inexperienced anesthetist (1), and vomiting with aspiration (5).

All too often certificates of death are written by interns or others not interested in accurate reports of puerperal deaths or unfamiliar with statistical implications. Yet at best the true importance of anesthesia is unknown under the present method of coding.

We have found that our placenta previa mortality was largely due to procrastination. In no case did initial hemorrhage cause death. In 18 out of 24 cases, repeated hemorrhage occurred before any treatment was instituted, a week or more elapsing in 12 cases. Transfusions were often inadequate.

Inspired by a visit to Philadelphia where analysis of puerperal deaths was going on, a similar study was begun in Brooklyn in 1936. With the excellent cooperation of the Commissioner of Health, the Maternity Center Division of the Visiting Nurse Association of Brooklyn and formal representation from every hospital, we have been able to get a perfect return of case histories. For three years we have assigned preventability of death, yet we long ago discovered that it is easy to do this only when a small committee of obstetricians sits in judgment. Time and again, at large meetings, we have been unable to form an opinion or have reversed our own previous decisions. Actually it is impossible to define preventability with scientific exactness, and it should be done that way or not at all. The very word implies a criticism not intended. Preventability statistics have served their purpose. Now we discuss controllable factors, planning and building up discussion and striving to establish standards of practice so far as that may be done, and using the word "preventable" only for stimulation of discussion.

It should be said that these meetings are well attended by obstetricians and general practitioners, interns and residents. No hospital or physician is identified in the discussion. Every physician in Brooklyn is invited and urged to attend, and everyone present has a voice, and a vote if one should be taken. The Committee on Analysis has become a committee of the entire profession, with its only purpose self-education. Once a year results are summarized and presented at an open meeting of the Brooklyn Gynecological Society.

It is idle, of course, to believe that any educational method will reach every physician, yet lessons learned by those present must eventually become widely diffused. And the knowledge that every puerperal death is under scrutiny operates for the benefit of the patient. It has been made clear that responsibility for the patient's welfare does not rest entirely with the physician. Not only do women have a right to expect every hospital to be a safe place for delivery, but the best interests of patient, hospital, and physician are served in no other way. More and more hospitals require consultation in all cases of long labor, hemorrhage, toxemia, and all operative procedures other than low forceps, and advice and help are available without fee, when the patient's physician feels that the situation should be managed that way.

That standards of practice become fairly well established after repeated group discussion is inevitable. The purpose of this paper is to call attention to the value of this teaching method as a source of inspiration for obstetrician and general practitioner alike.

Enough has been said to show that operative delivery, particularly cesarean section, is the heart of the Brooklyn problem. Any committee on analysis, able to inquire into all the circumstances of death, can just as readily outline its own situation. Certainly no problem can be solved until it is clearly stated. Yet this is not

enough. The educational value of committee discussion should not be overlooked. Individual interest on a large scale must be aroused, and every practitioner of obstetrics made to feel that he himself can make a worth-while contribution. This is essential. Education is continued by participation in the investigation and discussion of the all-important details appearing in the actual case records of puerperal death. The obstetric conference of the Committee on Analysis, wide open to every physician interested enough to attend, is an available and nearly perfect mechanism for that postgraduate education which we have found so difficult to provide for him. And, in the final analysis, solution of the medical problem lies in continued education.

256 JEFFERSON AVENUE

DISCUSSION

DR. BENJAMIN P. WATSON.—Each speaker has stressed that these committees in their discussions are not primarily concerned with individual responsibility or possible culpability, but only with the lessons that can be learned from any sins of omission or commission that may have occurred in the management of particular cases. They have wisely discarded the terms "preventability" and "nonpreventability" used in the original Academy of Medicine report, for around these two terms a great deal of the controversy, aroused by that report, raged. The terms were provocative. Looking back I, as one of the workers on that report, do not regret their use, for I believe that they, more than anything else, were responsible for the awakening of the medical profession to the necessity of looking further into this matter and for the establishment of the constructive work now being done by the Maternal Welfare Committees not only in Greater New York, but throughout the country. As both speakers have said, these meetings, open as they are to every member of the profession, are of real educational value and cannot but play a large part in the promotion of better obstetrics.

The reduction in maternal mortality in New York and throughout the country in the last three years has been most remarkable. I believe that the repeated statement of the problem in medical and lay meetings and journals has played a significant part in stimulating individual practitioners to do better work and to get better results. Any doctor who attends these Committee Meetings regularly and hears at meeting after meeting the same type of case discussed, the same mistake made in each case, the same want of foresight, and as a result, the same haste and confusion when emergency arises, must be better able to deal with that type of case when he himself encounters it.

Prenatal care resulting in the early detection and treatment of pregnancy toxemia, in the adequate treatment of cardiac and other complications, accounts for a large percentage of the total reduction in maternal mortality.

It is evident, however, from the facts given us by both speakers that a determined drive has to be made to inform the profession of the danger of operative obstetrics and of the necessity for making every provision for every possible emergency that may arise in its course. Dr. Gordon has told us how, as a result of their discussions in Brooklyn, standards of operative practice have been formulated, the necessity for close scrutiny of the indications for cesarean section, the importance of the type of anesthesia, the provision of blood by the presence of a donor or the accessibility of a blood bank, the proper preparations to make before the handling of a case of placenta previa, adherent placenta, or inversion of the uterus.

The fatalities in the course of and following operative obstetrics are usually the result of haste and confusion, because these provisions have not been made beforehand.

Society Transactions

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS

FIFTY-THIRD ANNUAL MEETING, EXCELSIOR SPRINGS, MO. SEPTEMBER 26 TO 28, 1940

The following papers were presented:

Home Delivery Service for Medical Students. Dr. Calvin R. Hannah, Dallas, Texas. (For original article, see page 417.)

Deep Cauterization of the Cervix. Drs. B. Z. Cashman and John S. Frank, Pittsburgh, Pa. (For original article, see page 379.)

A Skin Test for the Diagnosis of Pregnancy. Drs. Frederick H. Falls, V. C. Freda, and H. H. Cohen, Chicago, Ill. (For original article, see page 431.)

Transmigration of the Human Ovum. Dr. Q. U. Newell, St. Louis, Mo.

The Effects of Analgesia on the Newborn Infant. Dr. C. O. McCormick, Indianapolis, Ind. (For original article, see page 391.)

The Palatal Arch and the Pelvis. Drs. A. J. Rongy and A. B. Tamis, New York, N. Y.

Acidosis and Alkalosis in Obstetrics and Gynecology. Dr. W. T. Pride, J. R. Reinberger, and D. T. Holland, Memphis, Tenn. (For original article, see page 412.)

Pubertas Praecox Due to Ovarian Tumors. Dr. Clifford B. Lull, Philadelphia, Pa. (by invitation). (For original article, see page 445.)

Objections to Induction of Labor in Normal Pregnant Women. Dr. E. L. Cornell, Chicago, Ill. (For original article, see page 438.)

A Report of a Series of Complete Tears of the Perineum With Extension up the Posterior Vaginal Wall, Repaired by the Vaginal Flap Method. Dr. Ralph E. Campbell, Madison, Wis. (For original article, see page 403.)

The Theca Cone and Its Tropism Toward the Ovarian Surface, A Typical Feature of Growing Human and Mammalian Follicles. Dr. Erwin O. Strassmann, Houston, Texas. (For original article, see page 363.)

The Psychology of Pregnancy. Dr. Stuart B. Blakely, Binghamton, N. Y.

Re-operation: Analysis of 125 Gynecological Cases. Dr. E. Lee Dorsett, St. Louis, Mo.

Clinical Experience With Testicular Extract in Obstetrics and Gynecology. Dr. David Hadden, Oakland, Calif.

Actinomycosis of the Ovary. Dr. W. A. Coventry, Duluth, Minn. (For original article, see page 455.)

Nationality and Carcinoma of the Cervix. Dr. Frank R. Smith, New York, N. Y. (For original article, see page 424.)

Some Remarks About Maternal Mortality in the South. Presidential Address. Dr. James R. McCord, Atlanta, Ga. (For original article, see page 355.)

NEW YORK OBSTETRICAL SOCIETY

MEETING OF OCTOBER 8, 1940

The following papers were presented:

Menstruation and Urination Through a Clitorislike Structure. Drs. David N. Barrows and Winston N. Bloch. (For original article, see page 513.)

Puerperal Mortality in the Borough of Brooklyn, City of New York. Dr. Charles A. Gordon. (For original article, see page 535.)

A Study of Puerperal Mortality in New York City (1937-1940) with Special Reference to Preventive Factors. Dr. R. G. Douglas. (For original article, see page 529.)

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 7, 1940

The following papers were presented:

Report on Clinics—Woman's Medical College Hospital. Dr. Lewis C. Scheffey.

The Effect of Combined Administration of Chorionic Gonadotropin and the Pituitary Synergist on the Human Ovaries. Drs. Charles Mazer and Elkin Ravetz. (For original article, see page 474.)

Pubertas Praecox Due to Ovarian Tumor. Dr. Clifford B. Lull. (For original article, see page 445.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 18, 1940

The following papers were presented:

Amenorrhea and Sterility Caused by Bilateral Polycystic Ovaries. Dr. M. L. Leventhal. (For original article, see page 516.)

Report of a Case of Intravasation. Dr. E. W. Fischmann.

The Late Effects of the Toxemias of Pregnancy. Dr. John H. Moore, Grand Forks, N. D. (by invitation).

Some Observations on the Gynecic Employment of Equine Gonadotropins. E. C. Hamblen (by invitation). (For original article, see page 495.)

OBSTETRICAL SOCIETY OF BOSTON

MEETING OF NOVEMBER 19, 1940

The following paper was presented:

The Treatment of Pelvic Endometriosis. Dr. Walter T. Dannreuther (by invitation). (For original article, see page 461.)

PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 7, 1940

The following papers were presented:

Deep Cauterization of the Cervix. Drs. B. Z. Cashman and J. S. Frank. (For original article, see page 379.)

The Clinical Evaluation of Stilbestrol. Dr. Jos. A. Hepp.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Ectopic Pregnancy

Rojdestvenskaia, A. J.: The Etiology of Extra-Uterine Pregnancy, Surg., Gynec., Obst. **67**: 308, 1938.

The etiology of tubal pregnancy may depend on three factors: (1) the ovum developing its capacity for implantation before it reaches the uterus; (2) disturbed transportation of the ovum; (3) mechanical obstacles encountered by the ovum on its journey.

All three factors are closely connected with one another and therefore their distinction of one from another can be only approximate. However, the outstanding cause, apparently is the second factor, i.e., disturbed transportation of the ovum, for in all probability it may be the independent cause of tubal pregnancy, while the first and third factors, in particular (i.e., mechanical obstacles), play merely a relative part and must be accompanied by disturbed transportation, however slight, to cause tubal pregnancy.

The motor capacity of the tube depends to a great extent on the effect of the vegetative nervous system, which in its turn may be influenced by various emotions: fear of pregnancy, abortion, and the use of contraceptive measures.

From a study of 100 cases of tubal pregnancy, it is believed that the cause of the faulty implantation was the first factor in 10 per cent of cases, and the third in 76 per cent.

Among the mechanical causes, defective development of the tube of postembryonic nature seems to be of greatest importance.

Improvements in living conditions, less frequent occurrence of infectious diseases, and better working conditions for growing girls will reduce the percentage of extrauterine pregnancies.

WILLIAM C. HENSKE.

Villaca, Joao: Ectopic Pregnancy, Rev. de gynec. e. d'obst. **2**: 172, 1938.

The author presents a study of 20 cases of ectopic pregnancy. Three patients with abortion through the tube were operated upon and discharged cured; 7 instances of ruptured tubal pregnancy, all operated upon, with 1 death due to paralytic ileus; 1 patient with interstitial tubal pregnancy of eight months, 2 cases of lithopedion, 2 cases of abdominal pregnancy, 2 with supposed tumors of the ovary, which proved to be tubal pregnancies all operated upon; 1 of them with cirrhosis of the liver died postoperatively.

Thus of the 20 cases of extrauterine pregnancy reported, all patients were operated upon with two deaths.

MARIO A. CASTALLO.

Caccia, J. P.: Repeated Tubal Pregnancy, Semana méd **47**: 583, 1940.

From a review of the literature and a study of his own cases, Caccia concludes that recurrence of tubal pregnancy in the same woman takes place in about 4.14 per cent of cases. Such recurrences may be observed from two months to fifteen years after the first ectopic pregnancy. However, during this interval, normal intrauterine pregnancies may occur. The frequency of such normal gestations was 32 per cent. Hence, there is no justification for avoiding plastic operations on pregnant tubes because of the fear of a repetition of an ectopic pregnancy.

J. P. GREENHILL.

Olovson, T.: Bilateral Extrauterine Pregnancy, Acta obst. et gynec. Scandinav. **18:** 380, 1938.

Olovson reports a case of bilateral extrauterine gestation and collected 158 additional cases from the literature. He points out the necessity for exploring both tubes in all cases when operating for a tubal pregnancy.

J. P. GREENHILL.

Gaines, Collins, and Brown: Abdominal Pregnancy, South. M. J. **31:** 1278, 1938.

The histories of two patients with this relatively rare condition are presented in detail. The first was a 25-year-old primigravid negress who was admitted to the hospital in the seventh month of pregnancy. Beginning at about the second month, and persisting from time to time throughout the gestation, she experienced epigastric and right upper quadrant pain, gaseous eructation, and occasional vomiting. During this period there was a weight loss of 40 pounds. Fetal movements were first felt two months before admission and caused mild pains, and vomiting after meals. Three days previous to her arrival at the hospital they were accompanied by severe shooting pains in the upper abdomen, with dull aching pains and a sensation of heaviness in the pelvis. Abdominal enlargement corresponded to that of a full term gestation, and the baby lay in the upper half of the abdomen. To the left of the midline in the lower abdomen, and rising to the height of a four to five months' pregnancy, a spongy mass was felt. This was interpreted as uterine fundus. The cervix was firm, and there was no indication of dilatation or effacement, and the pelvis was empty. A clinical diagnosis of extrauterine pregnancy was confirmed by x-ray studies which demonstrated the fetus lying transversely across the upper abdomen just beneath the diaphragm. Under local anesthesia a left rectus incision was made. The placenta was found in the midline extending to the left and attached to the lower abdominal viscera and the uterus. The baby lay free in the peritoneal cavity, weighed 4 pounds and 2 ounces, and died seven hours later. During the postoperative course, there was hemorrhage upon 3 occasions, and the patient died on the thirteenth day.

The second patient was a 26-year-old colored multipara whose prenatal course was uneventful except for the fact that fetal movements had not been felt for one month before admission. The abdomen was the size of a full-term gestation, fetal heart tones were not audible. The pelvis was empty, and there was no cervical dilatation or effacement. Medical induction was not successful. She was discharged to prenatal clinic, and, because of toxemia, was readmitted for medical induction which again failed. Fetal movements and heart tones were absent. A fetal head was palpated at the umbilicus with crepitation. The Friedman test was negative. Surgical induction of labor was unsuccessful. Following an x-ray examination, a diagnosis of probable extrauterine gestation with dead fetus was made. At laparotomy, a full-term macerated fetus was found lying free in the peritoneal cavity. The abdomen was closed with drainage. Convalescence was essentially uneventful, and the patient was discharged on the fifteenth day.

ARNOLD GOLDBERGER.

Russell, B. P., Jr., and Black, W. T., Jr.: Primary Ovarian Pregnancy, South. Surgeon **9:** 114, 1940.

Primary ovarian pregnancy is a rare condition in which the fertilized ovum undergoes a certain stage of its development entirely within the ovary. In secondary ovarian pregnancy, the ovum, following its fertilization, undergoes some of its development in a nearby structure, usually the Fallopian tube, and then becomes implanted on the ovary. The literature contains 85 supposedly proved cases of primary ovarian pregnancy. The authors, in a review of the reports, found 52 cases in which the criteria for the primary condition existed as defined by Sutton. They report a new proved case of primary ovarian pregnancy.

The patient, 23 years of age, was pregnant for the second time. Following an amenorrhea of approximately eight weeks, there was nausea, severe lower abdominal pain, and vaginal bleeding. On admission temperature was 98.6° F., pulse 60,

and respiration 22. The patient perspired profusely and her skin was cold and clammy. There was some vaginal bleeding, and the chief complaints were nausea and severe lower abdominal pain. Laboratory studies showed: 3,570,000 red blood cells; 9.3 Gm. hemoglobin; 26,700 white cells, with 71 per cent polymorphonuclears. Because of an almost classic history of ectopic pregnancy, laparotomy was decided upon. Preliminary vaginal examination revealed a small uterus which was freely movable. There were no adnexal masses, but the right ovary was palpable. A soft mass was palpated in the cul-de-sac.

There was free blood in the peritoneal cavity, both tubes were normal and the right ovary was slightly cystic; a soft mass of bloody tissue in the cul-de-sac contained a placenta and fetus. In the left ovary there was a bleeding crater approximately 2 cm. in diameter, with adherent placental tissue. Left salpingo-oophorectomy was performed. The crown to heel length of the fetus was 78 mm., and its estimated age was 13 to 14 weeks. The Fallopian tube was 5 cm. in length and its lumen patent with masses of clotted blood at the fimbriated end. Microscopically, there was evidence of edema and hyperemia, but the mucosa was intact and no placental tissue was observed either in the tube or in the blood clot adherent to the fimbriae. Grossly, the lacerated portion of the ovary measured 2.2 cm. in diameter, and 1.2 mm. in depth. Histologic study of this area revealed edematous ovarian tissue, hemorrhage with fibrin clot, a convoluted layer of lutein cells, and chorionic villi within the ovarian tissue of adjacent areas.

It is suggested that all primary ovarian pregnancies develop upon the basis of pathologic changes in the ovary whereby ovulation is prevented by thickening of the theca or an unusually firm attachment of the ovum to the discus proligerus. In either case, there is retention of the ovum in the follicle. In this instance the ovarian stroma contained numerous follicle cysts. In the history of these patients, it is a noteworthy fact that periodic sterility is common.

To the accepted criteria for the establishment of the diagnosis of primary ovarian pregnancy, the authors wish to add the requirement that serial histologic sections of the tube on the affected side prove that rupture has not occurred.

ARNOLD GOLDBERGER.

Bittmann, O.: A Case of Simultaneous Tubal and Ovarian Pregnancy, Monatschr. f. Geburtsh. u. Gynäk. **110:** 17, 1939.

Bittmann reports the very rare if not unique observation of simultaneous extrauterine tubal and ovarian pregnancy in a 33-year-old woman. Both ova, implanted in the right tube and right ovary, were entirely separated from one another, so that the possibility of a tuboovarian pregnancy need not be discussed. The ovarian pregnancy was imbedded in a Graafian follicle; the right tubal pregnancy had its own corpus luteum in the left ovary. Histologic serial section of the resected right ovary gave no evidence of follicles with two or more ova.

Judging by this case as well as by another one of follicular pregnancy, one comes to the conclusion that a purely follicular pregnancy can only originate where the follicle has just burst and the opening caused by rupture is not yet closed, i.e., before fibrinoid transformation of the opening occurs. To be fertilized at all, the ovum must lie near the place of rupture which however must be very small. Moreover, the ovum must adhere in this place more firmly than usually, it must still be in firm communication with the granulosa cell stratum of the cumulus ovigerus; last, the inside pressure in the follicle must be lower than normal. An ovum fertilized in this place is very likely to have special energy toward implantation and nidation, for, although an ovum impregnated in this place also finds a nutritive epithelial medium, this is rather poor compared to the uterine and even to tubal mucosa. Histologically, the progress of such pregnancies is similar to conditions in placenta previa, especially in placenta previa cervicalis.

Based on the removed specimens it can be said that in this case the two fertilized ova must have been of different age, i.e., the result of different fecundations. The follicular pregnancy in the right ovary originated first. This leads one to consider whether one had to deal with a case of superfetation or of superfecundation. The author thinks that superfetation occurred in this case. The

difference in age of these two pregnancies, determined from the stage of ripeness of the follicle, cannot be considerable and hardly over three weeks.

The reported case is also a classical example of external migration as shown in the right tubal pregnancy which originated from the left ovary. After the relatively long travel from left ovary to right tube, the left tube being closed at its fimbriated end, the impregnated ovum was ready for nidation and implanted itself in the middle of the tube.

J. P. GREENHILL.

Stern, S. I.: Intramural Pregnancy, Gynéc. et obst. **38**: 193, 1938.

Intramural pregnancy is defined as a variety of ectopic gestation in which the ovum becomes implanted in the wall of the uterus, developing between the muscle layers. The author agrees with those writers who distinguish between intramural and interstitial pregnancy.

In a ten-year period, this condition was encountered twice in a series of 380 laparotomies performed for ectopic gestation, an incidence of 0.51 per cent. Of these one was a pure form of the condition, the other a mixed one. Both patients became pregnant again shortly after operative intervention, and were delivered of normal infants at term. The factors commonly discussed in connection with the etiology of ectopic gestation are reviewed.

The first patient, a 40-year-old multipara, had 13 full-term gestations and one miscarriage at three months, with a lapse of ten years since the previous gestation. Her last period occurred three weeks previously, and was late. She was admitted to the gynecologic service in a critical condition with signs of intra-abdominal hemorrhage. At operation the peritoneal cavity was full of blood, and at the region of the right uterine horn, there was a small nodular elevation near to a perforation. A small cavity, 4 mm. in diameter, the site of the implanted ovum, was filled with blood clot. The cornu was excised down to the mucosa, together with a portion of the tube, and peritonization was effected. On the fourteenth day postoperative, the patient was discharged in good condition. *Histologic diagnosis:* Intramural gestation, the site of implantation formed by the muscle layers of the uterus; villi take the stain well.

The second patient, aged 37 years, had one previous stillbirth. She was admitted to the hospital in shock, with signs of an intra-abdominal emergency. Following a two-month period of amenorrhea, and one week before admission, there was a bloody vaginal discharge followed by severe abdominal pain and syncope. At operation considerable blood was found in the peritoneal cavity, and in the isthmic portion of the left tube at the site of its origin from the uterus, there was an ectopic gestation. There was uneventful recovery of the patient. Histologic examination of the specimen revealed tubouterine pregnancy.

The author regretted his inability to make a detailed histologic study of the specimens, with the possibility of thus throwing more light upon the etiology of this condition. Ordinarily, the perforation occurs on the posterior surface of the fundus of the uterus; it is due to destruction of the muscle wall by placental villi.

ARNOLD GOLDBERGER.

Limpach, L., and Boy, J.: Tuberculosis of the Fallopian Tubes and Ectopic Pregnancy, Gynéc. et obst. **38**: 359, 1938.

Statistical reports indicate that 60 to 80 per cent of women with genital tuberculosis are sterile. Anatomic lesions, in addition to functional disturbances, are the factors chiefly responsible for this sterility. Should pregnancy occur, complications may ensue; of these, ectopic gestation is rare.

A 32-year-old nullipara who had been married for four years was admitted to the hospital with a history of amenorrhea of two months' duration, a bloody vaginal discharge upon one occasion, and violent lower abdominal pains. Ectopic pregnancy in left tube was suspected and the patient placed under observation. The Aschheim-Zondek test was positive. Nine days after admission acute lower abdominal pain recurred following the taking of castor oil. At laparotomy the peritoneal cavity was filled with blood, and there was a left hematosalpinx which

had ruptured in the region of the ampulla. The left adnexa were removed. Postoperative convalescence was uneventful.

Histopathologic examination revealed numerous double layered placental villi, and the characteristic features of an hyperplastic tuberculous salpingitis.

This case is unusual because pelvic tuberculosis rarely causes ectopic gestation; complete tubal occlusion with absolute sterility is the usual result.

ARNOLD GOLDBERGER.

Garcia, P., and Tisne, L.: Endometriosis and Tubal Pregnancy, Bol. Soc. chilena de obst. y ginec. **4**: 493, 1939.

The authors present a case of tubal pregnancy associated with endometriosis. They feel that the latter condition is more often a cause of ectopic pregnancy than is commonly realized and recommend the careful histologic study of tubes involved in this condition. The article contains several excellent microphotographs.

R. J. WEISSMAN.

Dubourc, G., and Mahon, R.: Importance of Histologic Examination of the Decidua in the Diagnosis of Extra-Uterine Pregnancy, Rev. franç. de gynéc. et d'obst. **34**: 42, 1939.

The authors call attention to the decidua in cases of extrauterine pregnancy and also to the fact that frequently pieces of decidua are considered to be an aborted ovum. Microscopic examination alone suffices to distinguish between decidua and ovum and hence, the differentiation between an intrauterine abortion and a pseudo-abortion of an ectopic pregnancy. Therefore, in all doubtful cases a histologic examination should be made of all the tissue which is expelled from the uterus or obtained by an exploratory curettement.

J. P. GREENHILL.

Dubrauszky and Martzy: Significance of the Friedman Pregnancy Test in the Diagnosis of Extra-Uterine Pregnancy, Klin. Wchnschr. **18**: 600, 1939.

The authors report the results of their findings in 69 cases of extrauterine pregnancy. Of these, 24 were acute and 45 chronic. They concluded from their studies that the Friedman pregnancy test has no great diagnostic value in the acute type of extrauterine pregnancy (i.e., with rupture). They arrive at this conclusion first, because the urgency of the case does not permit the time necessary for the carrying out of the test, and second, because of the inaccuracy of this test in the patient with the acute type of pathology. In the so-called chronic type, the Friedman test has some diagnostic value, but they caution against relying upon the test as a means of diagnosis. It should simply be used as a means of confirming other clinical and laboratory tests.

RALPH A. REIS.

Köberle, F.: Tubo-Uterine Abortion, Zentralbl. f. Gynäk. **63**: 1181, 1939.

Köberle reports the case of a 35-year-old woman who expelled a 35 mm. embryo from the vagina, one and one-half months after her last menses. Twelve days after the abortion the woman died. Autopsy revealed marked anemia due to intra-abdominal bleeding from a ruptured right Fallopian tube which was the seat of an ectopic pregnancy. Because of the location of the ovum in the isthmus of the tube, just at the junction with the uterus, the author assumes that during the course of the pregnancy the interstitial part of the uterus dilated and through this the fetus escaped into the vagina. The small rupture in the tube took place at the time when the fetus was expelled.

J. P. GREENHILL.

Items

American Board of Obstetrics and Gynecology

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted at Cleveland, Ohio, by the entire Board from Wednesday, May 28, to Monday, June 2, 1941, inclusive, prior to the opening of the annual meeting of the American Medical Association in Cleveland.

Formal notice of the time and place of these examinations will be sent each candidate several weeks in advance of the examination dates.

Candidates for *reexamination* in Part II must make written application to the Secretary's Office before April 15, 1941.

The Board requests that all prospective candidates who plan to submit applications in the near future request and use the new application form which has this year been inaugurated by the Board. The Secretary will be glad to furnish these forms upon request, together with information regarding Board requirements. Address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

This Board will hold its annual dinner for Diplomates, and others interested in the work of the Board, on Wednesday evening, June 4, 1941, at the Wade Park Manor Hotel, Cleveland, Ohio, immediately following the close of the Part II examinations, which will be conducted in Cleveland in the spring, immediately prior to the opening of the annual A. M. A. meeting.

The Journal of Clinical Endocrinology

A new monthly magazine devoted to this field, which is maintained by and issued for the Association for the Study of Internal Secretions, is being published by Charles C. Thomas of Springfield, Ill. It will cover the practical aspects of endocrine medicine, including diagnosis and therapy, symposia and reviews, original research. The Managing Editor is Dr. Milton Lee, of Boston, and there is a Publication Committee of well-known specialists and research workers. The new journal is designed to supplement the well-known and established *Endocrinology* which will continue to present articles on experimental research.